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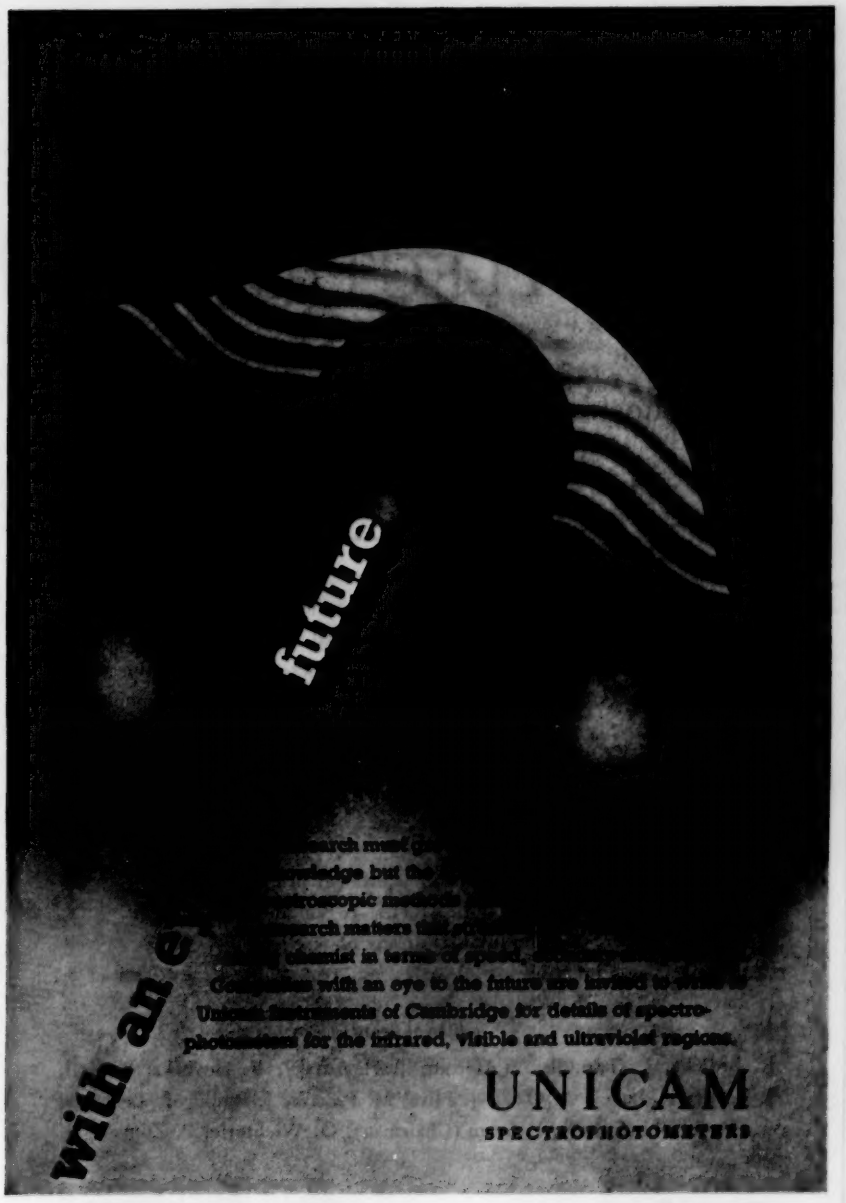
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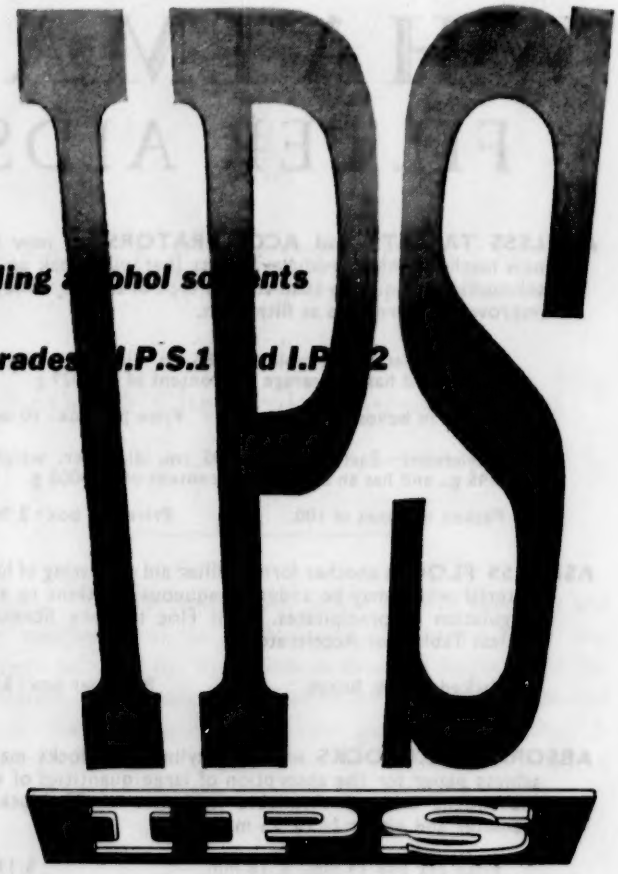

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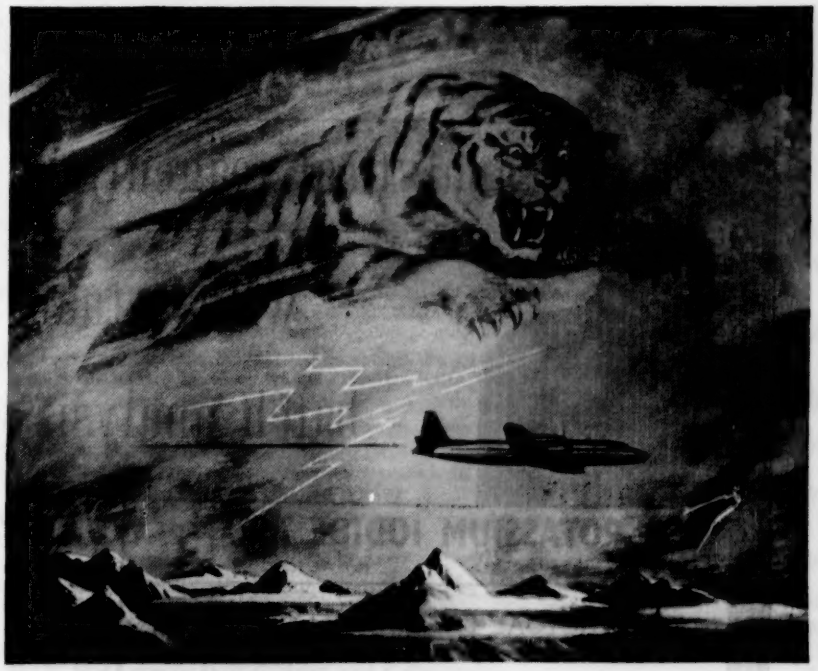

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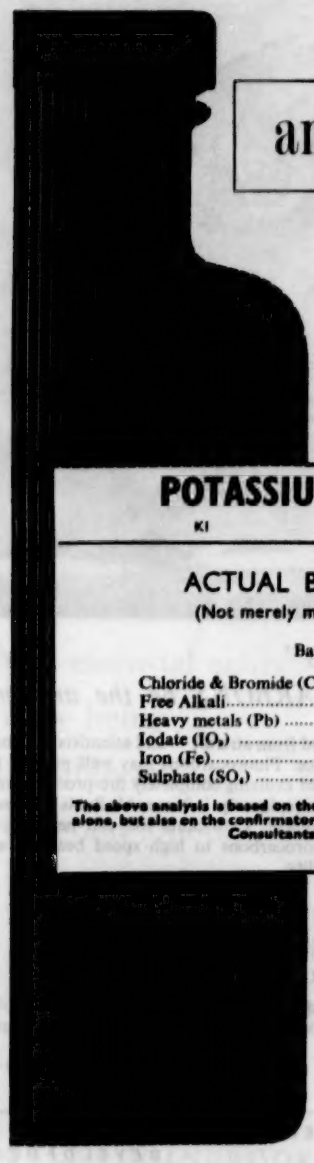

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Clark, H. C., and Odell, A. L., **3431**, **3435**.
Clark-Lewis, J. W. See King, F. E., **3384**.
Clemo, G. R., and Howe, R., **3552**.
Cornforth, J. W., Kauder, O., Pike, J. E., and Robinson, Sir R., **3348**.
Cousens, R. H., Ives, D. J. G., and Swaroopa, S., **3482**.
Craighead, P. W. See Panckhurst, D. J., **3395**.
Crawford, M., and Moore, G. W., **3445**.
Crawshaw, A., Henbest, H. B., Jones, E. R. H., and Wagland, A. A., **3420**.
Crimmin, W. R. C. See Holmes, F., **3467**.
Crombie, L., **3510**.
Cummins, J. A., and Tomlinson, M. L., **3475**.
Davison, W. H. T., and Christie, P. E., **3389**.
Dobson, N. A., and Raphael, R. A., **3558**.
Duffin, G. F., and Kendall, J. D., **3470**.
Edington, R. A., and Percival, E., **3554**.
Elvidge, J. A., and Linstead, R. P., **3536**.
Evans, E. A. See Braude, E. A., **3324**, **3331**, **3334**, **3337**.
Fairfull, A. E. S., Petrow, V., and Short, W. F., **3549**.
Fayez, M. B. E., Grigor, J., Spring, F. S., and Stevenson, R., **3378**.
Ficken, G. E., and Linstead, R. P., **3525**.
Fischer, E. See Frankel, M., **3441**, and Hirshberg, Y., **3313**.
Fodor, G., Tóth, J., and Vincze, I., **3504**.
France, H. See Baguley, M. E., **3521**.
Frankel, M., Wolovsky, R., and Fischer, E., **3441**.
French, C. M., and Harrison, D., **3513**.
Gibson, J. A. See Bell, F., **3560**.
Goldwhite, H., and Saunders, B. C., **3564**.
Grey, T. F. See Ames, D. E., **3518**.
Grigor, J. See Fayez, M. B. E., **3378**.
Harrison, D. See French, C. M., **3513**.
Hawkins, E. G. E., **3463**.
Henbest, H. B. See Crawshaw, A., **3420**.
Herington, E. F. G., and Kynaston, W., **3555**.
Hilton, M. L., Jones, A. S., and Westwood, J. R. B., **3449**.
Hirshberg, Y., Knott, E. B., and Fischer, E., **3313**.
Holmes, F., and Crimmin, W. R. C., **3467**.
Hough, L., and Taylor, T. J., **3544**.
Howe, R. See Clemo, G. R., **3552**.
Irving, H., and Mellor, D. H., **3457**.
Ives, D. J. G., and Swaroopa, S., **3489**.
Ives, D. J. G. See also Cousens, R. H., **3482**.
Janus, J. W., **3551**.
Johnson, J. D. A., **3322**.
Jones, A. S. See Hilton, M. L., **3449**.
Jones, E. R. H. See Crawshaw, A., **3420**.
Kauder, O. See Cornforth, J. W., **3348**.
Kendall, J. D. See Duffin, G. F., **3470**.
King, F. E., and Clark-Lewis, J. W., **3384**.
Knott, E. B. See Hirshberg, Y., **3313**.
Kohnstam, G. See Bensley, B., **3408**.
Kynaston, W. See Herington, E. F. G., **3555**.
Linstead, R. P., and Whalley, M., **3530**.
Linstead, R. P. See also Baguley, M. E., **3521**, Elvidge, J. A., **3536**, and Ficken, G. E., **3525**.
McOmie, J. F. W. See Chesterfield, J., **3478**.
Mellor, D. H. See Irving, H., **3457**.
Millson, M. F., and Robinson, Sir R., **3362**.
Miquel, J. F., Buu-Hoï, Ng. Ph., and Royer, R., **3417**.
Moore, G. W. See Crawford, M., **3445**.
Norymberski, J. K., and Woods, G. F., **3426**.
Odell, A. L. See Clark, H. C., **3431**, **3435**.
Panckhurst, D. J., Wilkins, C. J., and Craighead, P. W., **3395**.
Pandit, P. N. See Bradley, W., **3399**.
Percival, E. See Edington, R. A., **3554**.
Petrow, V. See Fairfull, A. E. S., **3549**.
Pike, J. E. See Cornforth, J. W., **3348**.
Pinder, A. R., and Robinson, Sir R., **3341**.
Randle, R. R., and Whiffen, D. H., **3497**.
Raphael, R. A., and Roxburgh, C. M., **3405**.
Raphael, R. A. See also Dobson, N. A., **3558**.
Robinson, Sir R. See Cornforth, J. W., **3348**, Millson, M. F., **3362**, and Pinder, A. R., **3341**.
Roxburgh, C. M. See Raphael, R. A., **3405**.
Royer, R. See Miquel, J. F., **3417**.
Rydon, H. N., and Tweddle, J. C., **3499**.
Saunders, B. C. See Goldwhite, H., **3564**.
Sayer, E. R. See Chesterfield, J., **3478**.
Shaw, J. I., and Stevenson, R., **3549**.
Shingu, T., Uyeo, S., and Yajima, H., **3557**.
Shipley, F. W., **3562**.
Short, W. F. See Fairfull, A. E. S., **3549**.
Spring, F. S. See Allan, G. G., **3371**, and Fayez, M. B. E., **3378**.
Stevenson, R. See Allan, G. G., **3371**, Fayez, M. B. E., **3378**, and Shaw, J. I., **3549**.
Strachan, W. S. See Allan, G. G., **3371**.
Swaroopa, S. See Cousens, R. H., **3482**, and Ives, D. J. G., **3489**.
Taylor, T. J. See Hough, L., **3544**.
Tomlinson, M. L. See Cummins, J. A., **3475**.
Tóth, J. See Fodor, G., **3504**.
Tweddle, J. C. See Rydon, H. N., **3499**.
Uyeo, S., and Yajima, H., **3392**.
Uyeo, S. See also Shingu, T., **3557**.
Vincze, I. See Fodor, G., **3504**.
Wagland, A. A. See Crawshaw, A., **3420**.
Wardlaw, W., **3569**.
Westwood, J. R. B. See Hilton, M. L., **3449**.
Whalley, M. See Baguley, M. E., **3521**, and Linstead, R. P., **3530**.
Whiffen, D. H. See Randle, R. R., **3497**.
Wilkins, C. J. See Panckhurst, D. J., **3395**.
Wolovsky, R. See Frankel, M., **3441**.
Woods, G. F. See Norymberski, J. K., **3426**.
Wyatt, P. A. H., **3438**.
Wyatt, P. A. H. See also Brayford, J. R., **3453**.
Yajima, H. See Shingu, T., **3557**, and Uyeo, S., **3392**.

Environmental Influences and the Colour of Some mero*Cyanines.*

By Yehuda Hirshberg, E. B. Knott, and Ernst Fischer.

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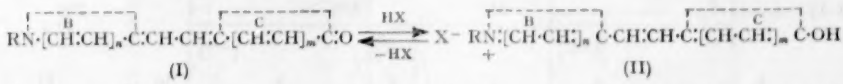
The effect of certain environmental factors on the absorption spectra of a series of dimethin*mero*cyanines has been examined. These include the degree of dilution, particularly in alcohols, the partial replacement of solvent ethanol by water, and temperature changes. It is shown that the varied behaviour of the dyes can, in general, be attributed to differences in their polarity. The most highly polar dyes exhibit two absorption bands in alcohols or aqueous alcohol, the long-wavelength band being attributed to the dye itself and the shorter-wavelength band to a quaternary cation formed between the solute and solvent. In general these bands are very sensitive to the environmental changes listed below.

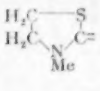
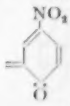
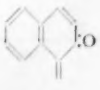
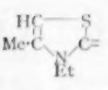
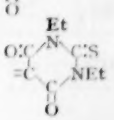
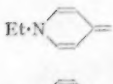
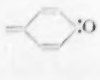
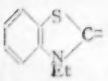
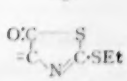
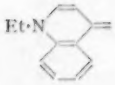
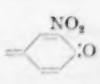
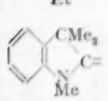
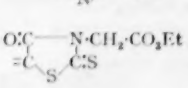
In the course of work on the photochromism of *spiro*pyrans (Hirshberg and Fischer, *J.*, 1954, 297; 1954, 3129) an investigation was undertaken of the effect of temperature changes and other factors on the colour of some dimethin*mero*cyanine dyes (I) because the structure of these dyes is related to that postulated for the coloured form of the photochromic compounds. The colour of related *mero*cyanines has been investigated and



(I) (II)

discussed extensively by Brooker *et al.* (*J. Amer. Chem. Soc.*, 1951, **73**, 5332, 5350) and by Knott (*J.*, 1951, 3038). All the compounds now examined are combinations of basic nuclei B and carbonyl-containing nuclei C, connected by a dimethin bridge in the general

Table I.

B nuclei	Designation	C nuclei	Designation	B nuclei	Designation	C nuclei	Designation
	I		1		V		5
	II		2		VI		6
	III		3		VII		7
	IV		4		VIII		8

form (I). For simplicity the various compounds will be denoted [B–C], where B and C stand for the numerals representing the two types of nuclei as given in Table I, *e.g.*, (III*a*) (p. 3320) is represented by [I–3].

The compounds investigated may be roughly divided into two groups according to their absorption spectra in ethanol in the visible range: (*a*) compounds possessing two bands about 100 mμ apart and (*b*) compounds possessing under all conditions only one main

TABLE 2. *Absorption spectra of group* (a) *dyes under various conditions.*

1 Compound	2 λ_1 (mμ)	3 λ_2 (mμ) [b]	4 $\varepsilon_2/\varepsilon_1$ [c]	5 Concn. (mg./l.)
[VII–2]	575	470	0·05	25
" in $COMe_2$	580, 550	—	—	8
[II–2]	600	470	0·05	35
" in MeOH	590	460	0·1	1·7
[II–3]	560	435	0·24	75
			2	1·5
" in $COMe_2$	610, 570	425	0·22	12
[IV–3]	600	450	0·26	90
			6·5	1·8
" in $COMe_2$	660, 615	440	7	1
[II–1]	560	400 (430 + 385) [e]	0·8	80
			6·3	8
" in $COMe_2$	620	400	0·55	170
[VI–3]	510	400	0·9	120
			3·5	6
[III–3]	515	400	1·1	130
			15	2·6
" in EtOH–MeOH (4 : 1)	515	—	—	15
" in $COMe_2$	585	390	—	—
[I–3]	500	385	1·1	165
			3·5	8·2
[I–1]	500	372	1·5	170
			3·2	8·5
[III–1]	515	390	1·7	250
			7	12·5

1 Compound	6 Effect of cooling on ratio $\varepsilon_2/\varepsilon_1$ [d]: original solution	6 Effect of cooling on ratio $\varepsilon_2/\varepsilon_1$ [d]: with TEA added	7 Hypsochromic shift of λ_1 [e]: cooling to −100° (mμ)	8 Hypsochromic shift of λ_1 [e]: EtOH–H_2O (1 : 1) (mμ)	9 EtOH–H_2O (1 : 9) [f] (mμ)	10 Hypsochromic shift of λ_2 in EtOH at −100° (mμ)
[VII–2]	None	None	5	—	20	<5
" in $COMe_2$	—	—	—	—	—	—
[II–2]	None	None	10	25	35	<5
" in MeOH	↑↑	—	—	—	—	—
[II–3]	—	↓	—	—	—	—
	↑↑	↓	28	30	60	—
" in $COMe_2$	—	—	—	—	—	—
[IV–3]	—	—	—	—	—	—
	↑	↓	40	35	80	−8
" in $COMe_2$	—	—	—	—	—	—
[II–1]	—	—	—	—	—	—
	↑	↓	35	20	55	−20
" in $COMe_2$	—	—	—	—	—	—
[VI–3]	—	—	—	—	—	—
	↑↑	None	~40	—	—	<5
[III–3]	—	—	—	—	—	—
	None	↓↓	30	30	65	<5
" in EtOH–MeOH (4 : 1)	↑↑	—	—	—	—	—
" in $COMe_2$	—	—	40	—	—	<5
[I–3]	—	—	—	—	—	—
	↑↑	↓	35	—	—	<5
[I–1]	—	—	—	—	—	—
	↑↑	↓	35	—	—	8
[III–1]	—	—	—	—	—	—
	↑	None	25	35	—	<5

[a] Solutions in ethanol at 26°, unless otherwise stated. [b] Identical with λ_2 in presence of excess of acid. [c] Figures in this column show the extent of the "dilution effect." No absolute data are given for ε, because of their dependence on environmental factors; however, their order of magnitude may be estimated from the fact that at the highest concentration in each case the optical density in 1-mm. cells is 0·5—1·5. [d] Unchanged by addition of triethylamine. [e] On cooling, this band is split into the two bands given, which seem to be differently affected by dilution, temperature, and pH. [f] Addition of H_2O increases the ratio $\varepsilon_2/\varepsilon_1$ in *all* cases; triethylamine annuls this effect. [g] ↑ = slight increase, ↓ = slight decrease, ↑↑ = strong increase, ↓↓ = strong decrease.

FIG. 1. *Dependence of the absorption spectra on the concentration. The optical densities were measured in 1-cm. cells for the medium concentration in each case, and in correspondingly shorter or longer cells at the higher or lower concentration, thus keeping constant the product of concentration and light path. The numbers in the upper left corner denote the compound, the figures accompanying the curves give the concentration in mg./l. of ethanol.*

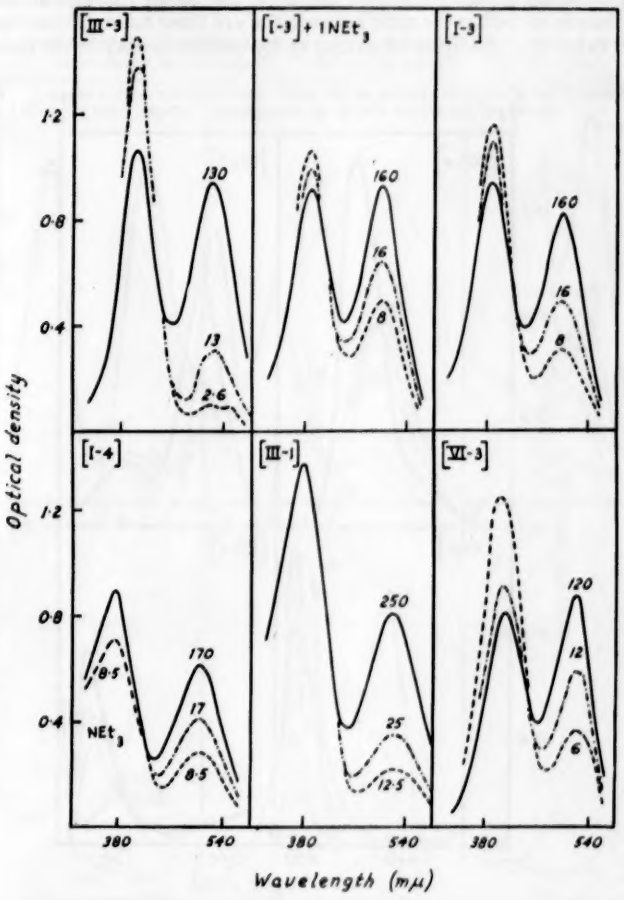


TABLE 3. *Absorption bands of nitro-derivatives in ethanol–methanol* (4 : 1) *at* 25°.

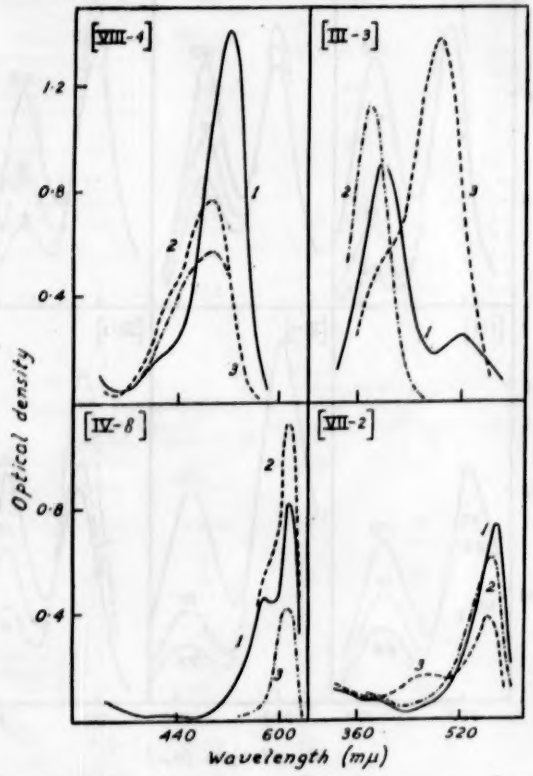
Compound	λ_1 (mμ)	$10^{-3}\varepsilon_1$	λ_2 (mμ)	$10^{-3}\varepsilon_2$	λ_3 (mμ)
[II–4]	520	175	390	116	320
[VII–4]	520	85	390	59	—
[VIII–4]	530	64	405	38	—
[II–5]	525	22	390	22	350
[III–5]	500	43	375	28	335
[VII–5]	525	30	395	26	370

Notes. In all cases neutral solutions show only a shoulder at λ_2, which increases somewhat on cooling, but forms a distinct band only with [III–5]. In presence of excess of HCl, only λ_3 is observed. No dilution effect was found with any compound. Cooling to −100° little affects λ_2, but shifts λ_1 hypsochromically by 15—25 mμ. Compounds containing nucleus 5 possess a third band at λ_2, which overlaps with λ_2 to some extent; $\varepsilon_2 \leqslant \varepsilon_3$; λ_3 is not affected by HCl. In compounds containing nucleus 4, λ_3 is probably still shorter and does not interfere with λ_2.

band, corresponding to the long-wavelength band in group (*a*). Group (*a*) comprises compounds with c nuclei 1—5 (Tables 2 and 3) and group (*b*) those with c nuclei 6—8 (Table 4). Compounds with c nuclei containing a nitro-group (4, 5) fall between the two groups, and will be described separately (Table 3).

In ethanol solutions of compounds of group (*a*) the molar extinction coefficients ε of the two visible bands, as well as the ratio between the ε of these bands, differ from compound to compound (Table 2). Addition of excess of hydrochloric acid in all cases suppresses

FIG. 2. *Dependence of the absorption spectra on the water content of the solvent ethanol. The numbers in the upper left corner denote the compounds.* (1-cm. cells.)



Compound	Curve 1	Curve 2	Curve 3
[VIII–4]	0% H_2O	90% H_2O	90% H_2O + 10 equiv. NEt_3
[III–3]	,,	,,	,, ,,
[IV–8]	,,	60% ,,	90% H_2O
[VII–2]	,,	50% ,,	50% H_2O + 100 NEt_3

the band at longer wavelength and enhances the band at shorter wavelength. The quantity of acid needed to cause the long band to disappear completely varies from 1 to 10 equivalents. Compounds belonging to group (*b*) are not affected even by much larger quantities of acid.

The absorption of compounds of group (*a*) is further affected by three factors—dilution, replacement of part of the solvent ethanol by water, and cooling.

The dependence of the absorption on the concentration of the solutions is shown in Fig. 1, in which the spectra for five representative compounds are given. Exact data for all compounds of this group are given in the fourth and fifth columns of Table 2. Dilution

of the dye solutions is seen to result in a considerable enhancement of the short-wave band and depression of the long-wave one. The extent of this effect again differs from compound to compound. In the presence of up to 10 equivalents of triethylamine the dilution effect is somewhat less pronounced.

The effect of addition of water to solutions of some *mero*cyanines has already been

FIG. 3. *Dependence of the absorption spectra on the temperature. The numbers in the upper left corner denote the compound. Solutions in ethanol.* (2·2-cm. cells.)

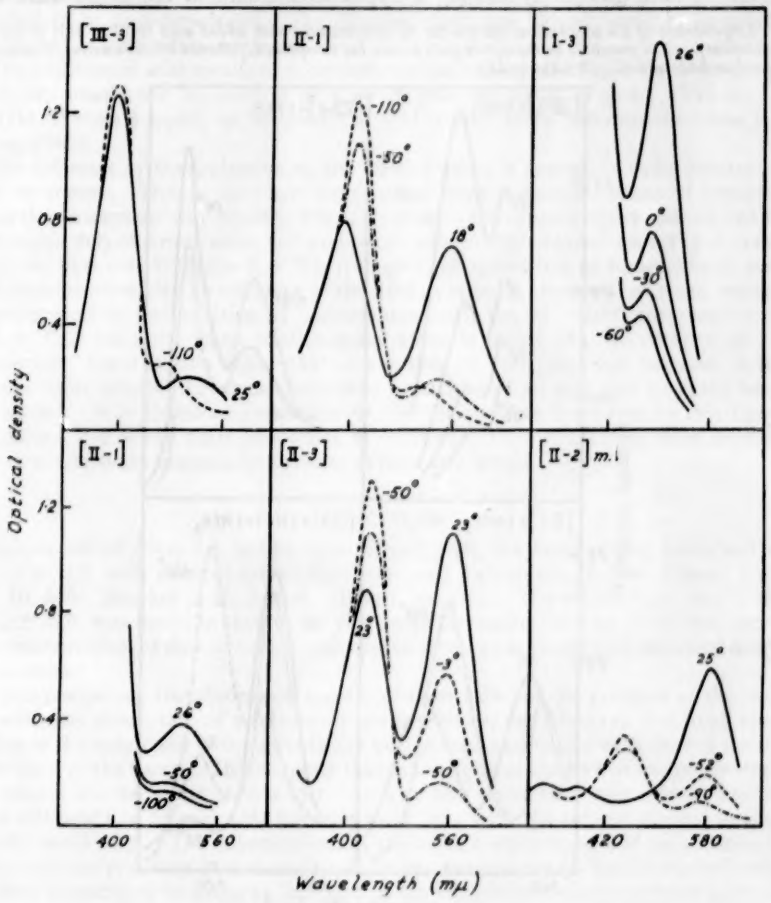


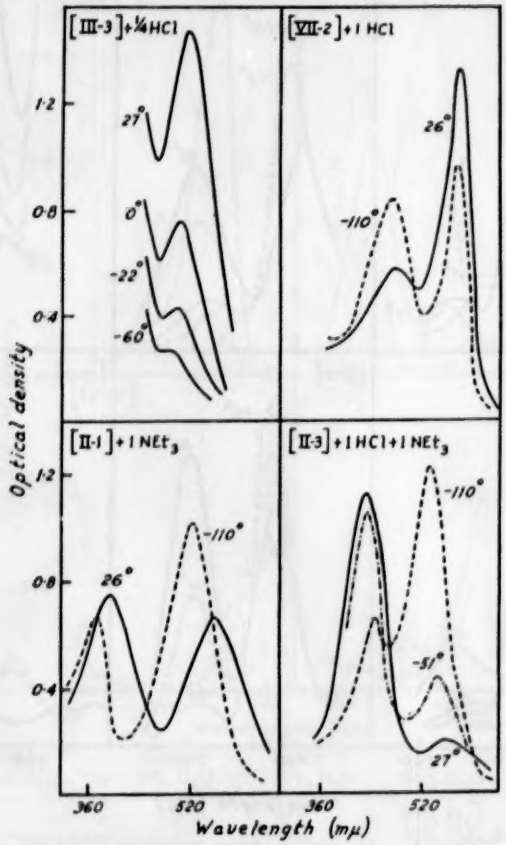
TABLE 4. *Absorption of compounds in group* (b).

Compound	$\lambda_{max.}$ (mμ) [a]	$10^{-3}\varepsilon_{max.}$	Effect of cooling: on ε	Effect of cooling: on λ (mμ)	Effect of H_2O: on ε	Effect of H_2O: on λ (mμ)
[I–8]	540 (520) [b]	85	↑	None	—	—
[II–7]	550	57	None	None	None	535
[II–8]	560, 530	164	Slight ↑	570	—	—
[III–8]	560 (530)	92	,, ↑	None	—	—
[IV–7]	630, 600, 580	109	None	None	—	—
[IV–8]	610, 470	76	Slight ↑	620	[c]	None
[VII–7]	530 (500)	38	—	—	[c]	None
[VIII–6]	490 (460)	134	None	None	↓	None

[a] Wavelength of longest visible band. [b] Wavelengths in parentheses denote inflexions. [c] With increasing percentage of H_2O, ε first rises, then falls.

reported by Brooker (*loc. cit*), who observed that the increased polarity of the solvent, resulting from an increased percentage of water, caused hypsochromic shifts of $\lambda_{max.}$ (corresponding to our long-wave band) and also changes in the extinction coefficient. Representative cases of the present observations are given in Fig. 2 and show two different phenomena: (1) For compounds of group (*a*) addition of water increases the ratio between the extinction coefficient ε_2 (of the short-wave band) and ε_1 (of the long-wave band). This effect is in all cases suppressed completely by even a small excess of triethylamine. (2) For compounds of both groups (*a*) and (*b*), a hypsochromic shift of the longer-wave band,

FIG. 4. *Dependence of the absorption spectra on the temperature with added acid* (HCl *or* HI) *or base* (*triethylamine*). *The numbers in the upper part denote the compound, followed by the number of equivalents of acid or base added.* (2·2-*cm. cells.*)



ranging from 0 to 80 mμ, occurs when 90% of the solvent ethanol is replaced by water. This shift is not affected by addition of excess of triethylamine. A similar effect has been described by Brooker (*loc. cit.*) and is a result of the increased polarity of the solvent containing water. Brooker also described cases in which gradual addition of water at first increased and then decreased ε. A similar case is shown in Fig. 2, compound [IV–8].

The effect of cooling on solutions of compounds in group (*a*) runs parallel to that of water described above; with decreasing temperature both the ratio $\varepsilon_2/\varepsilon_1$ and the hypsochromic shift of λ_1 increase steadily (Fig. 3).* The extent of both effects is indicated in

* A preliminary account of the cooling experiments has already been given (Hirshberg and Fischer, *J. Chem. Phys.*, 1954, **22**, 572).

columns 6, 8, and 11 of Table 2, again showing large variations among the compounds investigated. With compound [VII–2] there was even observed a reverse effect, ε_1 rising on cooling. This may be due to the same cause as the initial rise of ε_1 of [IV–8] on the addition of water (see Discussion). Methanol appears to be more effective than ethanol in increasing $\varepsilon_2/\varepsilon_1$ on cooling, as shown by compound [II–2]. The absorption of the latter remains unchanged when its solutions in ethanol are cooled, but is influenced strongly when a solution in a mixture of ethanol and methanol is cooled.

Since both dilution and cooling increase the ratio $\varepsilon_2/\varepsilon_1$ the two phenomena may be expected to be interdependent. The dilution effect was indeed found to be much more pronounced at higher temperatures.

The addition of acid results in occurrence of the cooling effect also for those compounds which are unaffected by cooling of their original solutions (Fig. 4: [VII–2], [III–3]. For [III–3] even $\frac{1}{4}$ equiv. of hydrochloric acid is seen to be sufficient to cause a strong cooling effect).

The influence of triethylamine on the cooling effect is analogous to its influence on the effect of water. Whereas at room temperature even a tenfold excess of triethylamine affects the absorption only slightly (Fig. 1), yet at $-100°$ even 1 equiv. annuls the cooling effect completely and even *raises* the long band considerably in some cases (Fig. 4, compound [II–1], cf. also col. 7, Table 2). When equivalent quantities of hydrochloric acid and triethylamine are added to solutions of the dyes in ethanol, the result at room temperature resembles that of the addition of hydrochloric acid, but at $-100°$ the result is almost equal to that obtained when triethylamine alone is added (Fig. 4, compounds [II–3]). Incidentally, these results show that a solution of the pure dye behaves differently from the same solution to which equivalent quantities of an acid and a (weak) base have been added. It is therefore impossible to liberate the free dye bases *in situ* from their hydriodides and study their properties in solution. This would have been desirable for those dyes which are unstable in the form of their free bases.

Discussion

Compounds of group (*a*), unlike those of group (*b*), are fairly strong bases and readily form salts (II) with mineral acids (Kiprianov and Petrun'kin, *J. Gen. Chem., U.S.S.R.*, 1940, **10**, 600; Brooker *et al.*, *loc. cit.*; Knott, *loc. cit.*). The equilibrium, dye + mineral acid $\rightleftharpoons$ salt, was found to shift to the right with increasing basicity of the dye, increasing total concentration of dye + acid, increasing relative concentration of acid, and decreasing temperature.

When comparing the absorption spectra of these salts, in the presence of the excess of acid, with the absorption of solutions of the free bases, one observes that in all cases the position of the only band of the salts in the visible region coincides with that of the shorter visible band of the bases. This suggests that in solutions of the dye bases the shorter-wave band should also be ascribed to a salt. In a system containing only solvent and solute, such a salt could be formed only between these two, with the solvent alcohol functioning as a very weak acid. The enhancement of the shorter-wave band and suppression of the longer-wave one resulting from the effect of various environmental factors on such solutions may then be ascribed to shifts to the right of the equilibrium, dye + solvent $\rightleftharpoons$ salt, in analogy to the equilibrium, dye + acid $\rightleftharpoons$ salt, described above.

Compound formation between dye and solvent may be expected to occur only with solvents (HX) containing an active hydrogen atom, such as water or alcohols. It was not possible to check this requirement experimentally, because of the difficulty in excluding from other solvents water and alcohols at concentrations comparable with those of the dyes in the solutions investigated.

A strong indication of the correctness of ascribing the short-wave band to the presence of the solute–solvent cation is given by the ratio $\varepsilon_2/\varepsilon_1$ (Table 2, col. 4) found for different dyes. As the basicity of the dye base increases so will the equilibrium (I) $\rightleftharpoons$ (II) be shifted to the right. If solute–solvent interaction occurs, then an increase in such basicity should lead to an increase in the ratio $\varepsilon_2/\varepsilon_1$.

As will be shown below, basicity and polarity of the dyes in general run parallel. The polarity of the dyes increases with increasing $-M$ effect of the nitrogenous nucleus (B) and with increasing $+M$ effect of the ketonic nucleus (C). The relative strengths of the $\pm M$ effects of most of the nuclei given in Table 2 have been determined by Brooker *et al.* (*loc. cit.*). Consequently, it is possible to arrange the dyes of Table 2 in a rough order of polarities. The order given in the Table is that of increasing values of $\varepsilon_2/\varepsilon_1$ in ethanol. It is found that with minor changes this same order agrees with the order of increasing polarities.

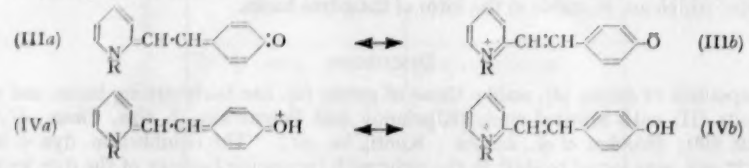
*mero*Cyanines derived from heterocyclic ketones (group *b*) are much less polar than those of group (*a*), as is known from absorption data, and indeed they show no tendency to combine with mineral acids or solvents and show no short band.

The suppression of the long-wave band of group (*a*) dye bases by dilution with water is somewhat stronger than by dilution with ethanol (cf. III–3, Figs. 1 and 2), indicating a higher stability of the cation hydroxide (II; X = OH) than of the cation ethoxide (II; X = OEt).

The hypsochromic shifts of λ_1 observed on cooling solutions of the dyes are as expected. Brooker *et al.* (1951, *loc. cit.*) have explained this on the basis of a decrease in the dielectic constant or of a stabilization of the orientation of the polar solvent molecules around the solute.

One would also expect the dielectric constant of the solvent to determine the extent to which the equilibrium solvent–solute is affected by the addition of a weak or moderately strong base. This would explain the much stronger effect of added triethylamine in suppressing the short-wave band in ethanol at −100° or in 90% water at 25°, as compared with ethanol at 25°.

The addition of a proton to the dye molecule (III) to give the cation (IV) will convert the dipolar extreme structure (III*b*) into a more stable cation (IV*b*), and the classical structure (III*a*) into a less stable cation (IV*a*). The effect of this will be twofold. The



increased separation of the energy levels of the extreme structures, as shown by the hypsochromic absorption shift, will decrease the resonance energy of the amidic resonance system. This loss of stability will be offset, however, by an increase in the resonance energy (aromatic) of the end nuclei as a result of the increased significance of (IV*b*) over (III*b*) in their respective hybrids. The net effect of proton addition to the dye base may thus either raise or lower the energy of the molecule depending upon the relative strengths of the two effects.

When the resonance system responsible for the long-wave band of the dyes is degenerate, the decrease of its resonance energy on proton addition will be at a maximum, falling away as the energetic symmetry of the resonance system is lost by increases or decreases in the polarity of the molecule. The greater the contributions, however, by the dipolar extreme structure in the particular solvent used, *i.e.*, the more polar the molecule, the more will the addition of a proton stabilize the molecule. Since all of the dyes of class (*a*) in polar solvents possess a dipolar extreme structure of lower energy than the classical extreme structure (Kiprianov and Petrun'kin, *loc. cit.*; *ibid.*, p. 613; Kiprianov and Timoshenko, *ibid.*, 1947, **17**, 1468; Brooker *et al.*, *loc. cit.*; Knott, *loc. cit.*), the net change in stability on proton addition will be increasingly positive with increasing dye polarity, *i.e.*, an increase in polarity results in an increase in basicity.

The nitro-derivatives described in Table 3 behave anomalously in showing no dilution effect and little fall in ε_1 on cooling. These dyes are more polar than the corresponding dyes without nitro-groups but their behaviour resembles more that of the least polar dye of group (*a*), *e.g.*, [VII–2] (cf. Table 2, col. 6). The reason for this loss of basicity on

nitration is probably connected with the increased acidity of nucleus (c). The dipolar extreme structure of dyes derived say from nucleus (5) will be stabilized by the additional resonance system (V*a* ◄► V*b*) resulting in an increase in polarity of the dye over its unnitrated analogue. However, the addition of a proton to $-O^-$ will increase the energetic asymmetry of this resonance system and this loss of resonance energy will discourage proton addition.

Experimental

Spectrophotometric Technique.—A Beckman model D.U. spectrophotometer was used throughout. The technique of work at reduced temperature has been described previously (Hirshberg and Fischer, *J.*, 1954, 297).

Solvents.—Great care was taken to exclude traces of acid from all the solvents used. Water, acetone, and methanol were distilled from potassium hydroxide; ethanol was refluxed over quicklime in the usual way.

Dyes and Dye Salts.—The dye [VII–2] was prepared according to the method of Witzinger and Wenning (*Helv. Chim. Acta*, 1940, **23**, 247); [II–3] and [VI–3] according to the method of Kiprianov and Petrun'kin (*loc. cit.*); [VII–5] according to the method of Kiprianov and Timoshenko (*loc. cit.*); [II–4], [VII–4], [VIII–4], [II–5], [III–5], [II–1], [I–1], [III–1], and [VIII–6] according to the method of Knott (*loc. cit.*); and [II–7], [V–7], and [VII–7] according to the method of Aubert, Knott, and Williams (*J.*, 1951, 2185). The dyes [I–8], [II–8], [III–8], and [IV–8] were prepared by condensation of the required 2(or 4)-methyl derivative of the heterocyclic quaternary salt with 3-ethoxycarbonylmethyl-5-ethoxymethylenerhodanine in alcoholic triethylamine and recrystallized from ethanol or benzene–ethanol.

1-*Ethyl*-1 : 4-*dihydro*-4-(4-*oxo*cyclo*hexadienylidene-ethylidene*)*quinoline* [IV–3].—Lepidine ethiodide (1·5 g., 0·005 mol.), *p*-hydroxybenzaldehyde (1·25 g., 0·01 ml.), methanol (10 c.c.), and piperidine (0·3 c.c.) were refluxed for 2 hr., and the mixture was chilled overnight. The styryl salt (1·55 g., 39%) which separated was heated on a steam bath with 2N-aqueous sodium carbonate until an oil separated and crystallized rapidly (1·2 g.). From water, then from methanol–ether, it formed deep blue needles of indefinite m. p., becoming bronze-coloured on drying at 95°/15 mm. (Found: C, 65·8; H, 7·4; N, 3·95. $C_{19}H_{17}ON,H_2O$ requires C, 65·7; H, 7·2; N, 4·05%).

1-*Ethyl*-1 : 2-*dihydro*-2-(4-*oxo*cyclo*hexadienylidene-ethylidene*)*pyridine* [I–3].—α-Picoline ethiodide (2·5 g., 0·01 ml.), *p*-hydroxybenzaldehyde (2·5 g., 0·02 mol.), methanol (15 c.c.), and piperidine (0·5 c.c.) were refluxed for 3 hr. The yellow crystals (2·3 g., 66%) of **2-p-*hydroxystyrylpyridine ethiodide*** which separated formed yellow needles, m. p. 248°, from methanol (Found: I, 36·0. $C_{15}H_{16}ONI$ requires I, 36·1%). It (2·0 g.) was dissolved in hot 2N-aqueous sodium carbonate (25 c.c.) and the solution on chilling gave orange needles. From hot water (solution red when hot, yellow when cold) it formed yellow needles, m. p. 90°. On drying *in vacuo* over potassium hydroxide the needles became red (m. p. indefinite) but in moist air they regained their original colour (Found: C, 54·4; H, 7·9; N, 4·3. $C_{15}H_{15}ON,6H_2O$ requires C, 54·0; H, 8·1; N, 4·2%).

1-*Ethyl*-1 : 4-*dihydro*-4-(4-*oxo*cyclo*hexadienylidene-ethylidene*)*pyridine* (III–3) was obtained similarly. The red plates which separated from the sodium carbonate solution on chilling formed light purple plates from water. They formed maroon needles, m. p. 207°, from methanol–ether (Found: C, 60·6; H, 8·1; N, 4·9. $C_{15}H_{15}ON,4H_2O$ requires C, 60·6; H, 7·75; N, 4·7%).

The intermediate **4-p-*hydroxystyrylpyridine ethiodide*** formed flat reddish plates, m. p. 193°, from ethanol (Found: I, 36·3. $C_{15}H_{16}ONI$ requires I, 36·1%).

The authors are indebted to Dr. Anna Weizmann for a sample of compound [II–2] and to Mrs. Nelly Castel for technical assistance.

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2 : 4 : 6-*Tri-iodophenyl* iso*Cyanate as a Reagent for Hydroxy- and Amino-groups.*

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2 : 4 : 6-Tri-iodophenyl *iso*cyanate gives with many alcohols urethanes which are useful for identification, but it is useless for separation of alcohols from beeswax owing to solubility of the long-chain alkyl derivatives.

THE alcohols of acid-free Benguela beeswax are only partly obtained as hydrogen phthalates when the acid-free wax is treated with phthalic anhydride–pyridine. In an attempt to isolate the alcohols as derivatives insoluble in the esters and hydrocarbons forming the wax residuum, 2 : 4 : 6-tri-iodophenyl *iso*cyanate was chosen as reagent. Though this proved useful for the detection and identification of alcohols, the original purpose remains unfulfilled. Beeswax reacted with the *iso*cyanate in light petroleum, but it was impossible to determine whether the precipitate obtained on concentration and cooling the solution comprised only the 2 : 4 : 6-tri-iodophenylurethanes or contained admixed beeswax esters and/or hydrocarbons ; some of the wax compounds also separate under these conditions and recrystallisation was excluded by the nature of the problem.

Methyl and ethyl 2 : 4 : 6-tri-iodocarbanilate were relatively insoluble in cold light petroleum, but, on ascending the homologous series of primary alcohols, the solubility increased in all those solvents, including petroleum, in which beeswax is reasonably soluble. The curve relating melting point with the number of carbon atoms in the normal alkyl chain showed alternation.

Normal and branched purely aliphatic primary alcohols with 2 : 4 : 6-tri-iodophenyl *iso*cyanate readily give crystalline products; primary aralkyl alcohols behave similarly, but, whereas allyl and cinnamyl alcohol formed crystalline products in a few minutes, the unsaturated oleyl alcohol in light petroleum gave only a jelly, as also did 2-hydroxyethyl laurate. Simple alkoxy-ethanols formed the urethanes, but ethanolamine gave *N*-2-hydroxyethyl-*N'*-(2 : 4 : 6-tri-iodophenyl)urea, indicating the greater reactivity of the amino-group towards the reagent. The nature of this derivative was inferred from the high melting point and the insolubility in dilute acid. The derivatives from dimethylamino- and diethylamino-ethanol were of course urethanes, being much lower-melting and soluble in dilute hydrochloric acid.

Simple secondary alcohols react readily, and (−)-menthol gave a derivative on more prolonged heating; ethyl lactate, octan-2-ol, 1-phenylethanol, borneol, and diphenylmethanol failed to react in light petroleum (b. p. 60—80°), though in absence of solvent they gave urethanes in 30 minutes at 150°.

No derivative of a tertiary alcohol has been obtained. Diacetone alcohol at 150° gave a white insoluble solid which appeared to be the diurea.

Phenols react only in the absence of a solvent at 150, the products, in general, being insoluble or, if crystalline, unsuitable for identification of the phenols.

Simple glycols react readily in the absence of a solvent, but the products are very insoluble. Diethylene glycol in light petroleum (b. p. 100—120°) (only a very dilute solution is possible) reacted at 100° to give the diurethane.

*iso*Cyanates often yield the corresponding symmetrically disubstituted ureas when treated with water, some of the amine first formed reacting with the unchanged *iso*cyanate. When 2 : 4 : 6-tri-iodophenyl *iso*cyanate was boiled with aqueous pyridine, 2 : 4 : 6-tri-iodoaniline was obtained. Presumably the insolubility of the amine prevented its reaction with unchanged *iso*cyanate. The diurea was, however, obtained as a by-product in the formation of the *iso*cyanate from 2 : 4 : 6-tri-iodoaniline and carbonyl chloride in toluene, and probably when the *iso*cyanate and 2 : 4 : 6-tri-iodoaniline were heated in toluene for some hours.

Light petroleum solutions of the *iso*cyanate react readily with primary aromatic amines,

but the products are not easily crystallised. Secondary amines such as morpholine, piperidine, and diethylamine reacted readily in light petroleum. Diphenylamine appeared to give no product even after 12 hours in this solvent, but gentle heating in absence of a solvent for about three minutes in the molten condition led to the urea.

Experimental

2 : 4 : 6-*Tri-iodophenyl* iso*Cyanate*.—A current of carbonyl chloride was passed through a wide entry-tube into a solution of 2 : 4 : 6-tri-iodoaniline (177 g.) (Hantzsch, *Ber.*, **1903**, **36**, 2070; recrystallised from toluene) in toluene (2124 ml.) on a steam-bath, with stirring under reflux, for 6 hr. The solution was left overnight, then heated for 3 hr. The carbonyl chloride and about 1250 ml. of toluene were distilled off, later under reduced pressure, and the *s*-di-(2 : 4 : 6-tri-iodophenyl)urea (20 g.) was filtered off. Evaporating the filtrate to dryness gave crude 2 : 4 : 6-*tri-iodophenyl* iso*cyanate*, which, recrystallised from light petroleum (2·8 l.) (b. p. 60—80°), formed faintly coloured needles, m. p. 129° (147 g., 79%) (Found : C, 16·85; H, 0·5; N, 2·8. $C_7H_2ONI_3$ requires C, 16·9; H, 0·4; N, 2·8%), moderately soluble in toluene and acetone and

Urethanes (*from alcohols and phenols*) *and ureas* (*from amines and hydroxy-amines*).

Alcohol	Formula	M. p.	Solvent *	Found (%) C	H	N	Calc. (%) C	H	N
MeOH	$C_8H_5O_2NI_2$	209°	Pet B	18·65	1·4	3·0	18·15	1·1	2·65
EtOH	$C_9H_7O_2NI_2$	194	,,	20·2	1·6	2·7	19·9	1·5	2·6
Pr^{n}OH	$C_{10}H_9O_2NI_2$	162	,,	22·0	2·0	2·6	21·5	1·8	2·5
Bu^{n}OH	$C_{11}H_{11}O_2NI_2$	151	,,	23·4	2·2	2·6	23·1	2·1	2·45
n-C_5H_{11}·OH	$C_{12}H_{13}O_2NI_2$	120	,,	24·2	2·55	2·5	24·6	2·4	2·4
n-C_7H_{15}·OH	$C_{14}H_{17}O_2NI_2$	105	,,	27·9	3·1	2·3	27·4	2·9	2·55
n-C_8H_{17}·OH	$C_{15}H_{19}O_2NI_2$	107	,,	29·1	3·45	2·3	28·7	3·2	2·2
n-C_9H_{19}·OH	$C_{16}H_{21}O_2NI_2$	105	,,	29·7	3·3	2·35	29·95	3·4	2·2
n-$C_{10}H_{21}$·OH	$C_{17}H_{23}O_2NI_2$	108	,,	31·4	3·8	2·4	31·1	3·7	2·1
n-$C_{12}H_{25}$·OH	$C_{19}H_{27}O_2NI_2$	112	,,	33·1	4·1	2·1	33·4	4·1	2·05
n-$C_{16}H_{33}$·OH	$C_{23}H_{35}O_2NI_2$	108	,,	37·8	5·1	2·0	37·35	4·9	1·9
Bu^{t}OH	$C_{11}H_{12}O_2NI_2$	140	Pet A	23·2	2·0	2·6	23·1	2·1	2·45
$CHEt_2$·CH_2·OH	$C_{13}H_{16}O_2NI_2$	77	,,	26·3	2·6	2·4	26·0	2·7	2·3
CH_2Ph·OH	$C_{14}H_{10}O_2NI_2$	175	Pet B	28·15	1·9	2·5	27·8	1·65	2·3
CH_2Ph·CH_2·OH	$C_{15}H_{12}O_2NI_2$	170	Pet A	29·3	2·2	2·5	29·1	1·9	2·3
Ph·$[CH_2]_3$·OH	$C_{16}H_{14}O_2NI_2$	135	Pet C	30·7	2·35	2·6	30·3	2·2	2·2
MeO·CH_2·CH_2·OH	$C_{10}H_{10}O_3NI_2$	146	Pet A	21·3	1·9	2·8	20·9	1·7	2·4
EtO·CH_2·CH_2·OH	$C_{11}H_{12}O_3NI_2$	142	Pet B	23·0	2·3	2·5	22·5	2·0	2·4
p-MeO·C_6H_4·CH_2·OH	$C_{15}H_{12}O_3NI_2$	176	,,	28·7	2·2	2·2	28·3	1·9	2·2
NMe_2·CH_2·CH_2·OH	$C_{11}H_{13}O_2N_2I_3$	115	Pet C	—	—	4·8	—	—	4·8
NEt_2·CH_2·CH_2·OH	$C_{13}H_{17}O_2N_2I_3$	131	Pet A	25·8	2·8	4·7	25·4	2·8	4·6
O·CH_2·CH_2·CH_2·CH·CH_2·OH	$C_{13}H_{12}O_3NI_3$	137	Pet B	24·4	2·1	2·5	24·0	2·0	2·3
CH_2:CH·CH_2·OH	$C_{10}H_9O_2NI_2$	178	Pet A	22·1	1·7	2·6	21·6	1·4	2·5
CHPh:CH·CH_2·OH	$C_{16}H_{12}O_2NI_2$	190	Pet B	30·9	2·8	2·25	30·4	1·9	2·2
Pr^{i}OH	$C_{10}H_{10}O_2NI_2$	180	,,	21·8	2·1	2·7	21·5	1·8	2·5
CHMeEt·OH	$C_{11}H_{12}O_2NI_2$	161	Pet A	23·35	2·2	2·5	23·1	2·1	2·45
C_6H_{13}·CHMe·OH	$C_{15}H_{20}O_2NI_2$	98	Aq. EtOH	28·9	3·4	—	28·7	3·2	—
C_6H_{11}·OH	$C_{13}H_{14}O_2NI_2$	145	Pet A	26·5	2·8	2·5	26·0	2·7	2·3
CHPhMe·OH	$C_{15}H_{12}O_2NI_2$	179	Aq. pyridine	29·3	2·3	2·6	29·1	1·9	2·3
Borneol	$C_{17}H_{20}O_2NI_2$	171	Pet B	31·7	3·4	—	31·3	3·1	—
(−)-Menthol	$C_{17}H_{26}O_2NI_2$	143	,,	31·05	3·65	2·4	31·2	3·4	2·1
$CHPh_2$·OH	$C_{20}H_{14}O_2NI_2$	195	EtOH	35·2	2·1	2·1	35·2	2·1	2·1
HO·CHMe·CO_2Et	$C_{12}H_{13}O_4NI_2$	154	Pet B	23·5	2·1	2·3	23·4	1·95	2·3
PhOH	$C_{12}H_9O_2NI_2$	181	,,	—	—	2·3	—	—	2·4
$O(CH_2$·CH_2·OH$)_2$	$C_{14}H_{14}O_5N_2I_6$	222 †	Anisole	20·1	1·4	2·8	19·6	1·3	2·55
Amine									
NH_2Me	$C_8H_7ON_2I_3$	285—290 †	Aq. pyridine	18·45	1·2	5·45	18·2	1·3	5·3
NH_2Ph	$C_{13}H_9ON_2I_3$	>271	,,	26·4	1·5	4·8	25·4	1·5	4·7
p-EtO·C_6H_4·NH_2	$C_{15}H_{13}O_2N_2I_3$	277 †	,,	28·6	2·1	4·4	28·4	2·05	4·4
o-MeO_2C·C_6H_4·NH_2	$C_{15}H_{11}O_2N_2I_3$	>285	BuOH	27·8	1·7	4·7	27·8	1·7	4·3
$O<(CH_2$·$CH_2)_2>NH$	$C_{11}H_{11}O_2N_2I_3$	262	EtOH	23·1	2·2	—	22·6	1·89	—
$CH_2<(CH_2$·$CH_2)_2>NH$	$C_{12}H_{13}ON_2I_3$	205	,,	24·7	2·4	—	24·7	2·2	—
$NHEt_2$	$C_{11}H_{13}ON_2I_3$	163	Aq. EtOH	23·6	2·6	4·9	23·2	2·3	4·9
$NHPh_2$	$C_{19}H_{13}ON_2I_3$	210	,,	34·65	2·25	—	34·2	1·95	—
NH_2·CH_2·CH_2·OH	$C_9H_9ON_2I_3$	260	BuOH	19·5	1·75	5·1	19·4	1·6	5·0

* Pet = light petroleum, b. p.: A = 60—80°; B = 80—100°; C = 100—120°. † Decomp.

soluble to the extent of about 1% in cold and about 5—6% in hot light petroleum (b. p. 60—80°). The *urea* was insoluble in all the solvents tried, but, as obtained, formed minute needles unmelted at 300° (Found : C, 16·9; H, 0·6; N, 3·1. $C_{14}H_6ON_2I_6$ requires C, 17·1; H, 0·6; N, 2·9%).

Urethanes.—General method. The alcohol in slight excess was added to a hot solution of the *iso*cyanate (0·5 g.) in light petroleum (b. p. 60—80°; 30 ml.) and heated on the steam-bath for 1 hr. In some cases it was necessary to concentrate the solution slightly afterwards in order to isolate the product. Departures from these conditions for secondary alcohols, glycols, and certain amines are mentioned in the theoretical portion. *Products* are tabulated.

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Alkenylation with Lithium Alkenyls. Part IX. Synthesis of Dimethylbutadienecarboxylic Acids.*

By E. A. Braude and E. A. Evans.

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2-Hydroxy-2 : 4-dimethylpent-3-en-1-al has been prepared in high yield from *iso*butenyl-lithium and pyruvaldehyde diethyl acetal and has been converted into 2 : 4-dimethylpenta-2 : 4-dienoic acid by a variety of routes. The transformations involved, and the spectral properties of the products, are discussed.

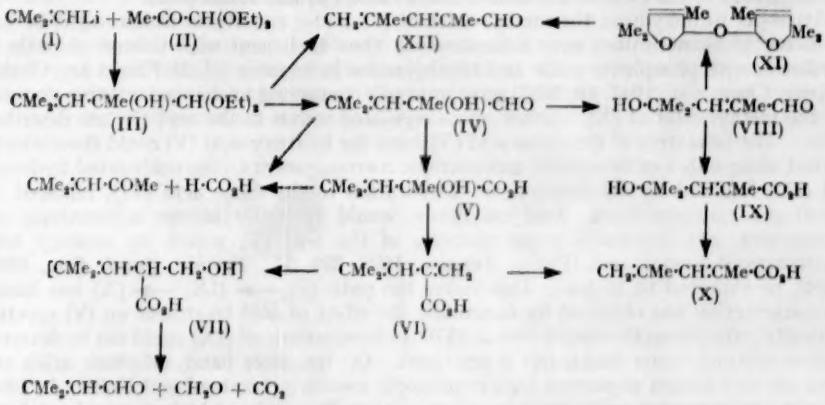
The aim of the work described in this paper was the synthesis of a buta-1 : 3-diene-2-carboxylic acid. Except for one cyclic derivative which has been described recently (Part VIII, Braude and Evans), diene acids of this type appear to be almost unknown, although the occurrence of such structures has been postulated in certain natural products, particularly α-longinecic and ridellic acids (Adams, Govindachari, Looker, and Edwards, *J. Amer. Chem. Soc.*, 1952, **74**, 700; Adams and Van Duuren, *ibid.*, 1953, **75**, 4638). The preparation of simple analogues and an examination of their chemical and physical properties would therefore be of interest.

A previous attempt to obtain an open-chain 1 : 3-diene-2-carboxylic acid directly from a lithium alkadienyl intermediate was unsuccessful (Part VIII, *loc. cit.*), but an alternative approach, involving the use of a more stable lithium alkenyl, appeared to be that outlined in (I) —► (VI). This sequence of reactions has been carried out, but the desired product, 4 : 4-dimethylbuta-1 : 3-diene-2-carboxylic acid (VI), proved to be highly unstable and to undergo prototropic rearrangement with great ease to the isomeric 1 : 3-dimethylbuta-1 : 3-diene-1-carboxylic acid (2 : 4-dimethylpenta-2 : 4-dienoic acid) (X).

The preparation of *iso*butenyl bromide and its conversion into *iso*but-1-enyl-lithium (I) (Braude and Timmons, Part I, *J.*, 1950, 2000; Braude and Coles, Part III, *J.*, 1950, 2012) has been simplified and considerably improved. Reaction of *tert.*-butyl alcohol with bromine gave 1 : 2-dibromo*iso*butane directly, without isolation of *iso*butene [cf. Pansevich-Kolyada and Prilezhaev, *J. Gen. Chem.* (*U.S.S.R.*), 1951, **21**, 517; *Chem. Abs.*, 1951, **45**, 8442; Andrews and Keefer, *J. Amer. Chem. Soc.*, 1953, **75**, 3557]. Dehydrobromination is best effected by potassium hydroxide in ethylene glycol; after careful refractionation, the *iso*butenyl bromide obtained in this way attacks lithium in ether exothermally after an induction period of only a few minutes, in contrast to the rather sluggish reaction observed previously (Parts I and III, *loc. cit.*; Braude and Timmons, *J.*, 1953, 3131). This is undoubtedly due to the fact that the present procedure gives the bromide in an even higher state of purity, and further illustrates the effect, previously noted, of minute traces of impurities on the metallation reaction. In a recent series of papers, Normant (*Compt. rend.*,

* Part VIII, *J.*, 1954, 607.

1954, **239**, 1510, 1811; 1955, **240**, 314, 440, 631, 1111) has reported that vinyl halides can be converted into Grignard reagents in high yields in tetrahydrofuran, though few details are disclosed. In our hands, *iso*butenyl bromide failed to react with magnesium under such conditions, in agreement with previous experience (Part I, *loc. cit.*). Addition of *iso*butenyl-lithium to pyruvaldehyde diethyl acetal (II) afforded the hydroxy-acetal (III; R = Et); the yield (64%) was considerably higher than those achieved earlier with this lithium alkenyl and the extent of the Wurtz side-reaction giving tetramethylbutadiene was considerably reduced. Rather lower yields of the hydroxy-acetal (III; R = Me) were obtained from pyruvaldehyde dimethyl acetal.



Preliminary experiments showed that the hydroxy-acetals (III) and their hydrolysis products were very much more sensitive to acid treatment than the corresponding ketal prepared from diacetyl monoketal (Braude and Timmons, 1953, *loc. cit.*). By treatment with 2% aqueous tartaric acid at room temperature under carefully controlled conditions (cf. Lunt and Sondheimer, *J.*, 1950, 3361), the hydroxy-aldehyde (IV) was, however, obtained in excellent yield (93%). It exhibited ultraviolet-light absorption characteristic of an α-hydroxy-aldehyde group ($\lambda_{max.}$ 2830 Å, ε 65), but failed to give a semicarbazone, and no 2 : 4-dinitrophenylhydrazone was formed in pyridine solution, in contrast to the behaviour of the corresponding methyl ketone (Braude and Timmons, 1953, *loc. cit.*). Treatment with Brady's reagent gave the derivative of the isomeric aldehyde (VIII) (see below).

Oxidation of the hydroxy-aldehyde (IV) with silver oxide (cf. Kuhn and Trischmann, *Annalen*, 1951, **573**, 58) furnished the hydroxy-acid (V), together with mesityl oxide and ββ-dimethylacraldehyde, isolated and identified as the 2 : 4-dinitrophenylhydrazones, as well as formic acid. The hydroxy-acid (V) itself is very unstable and could not be obtained pure, but was converted into the methyl ester with diazomethane. The mesityl oxide and formic acid are probably derived from the hydroxy-aldehyde (IV) by reverse aldol reaction and subsequent oxidation of the formaldehyde; this would be analogous to the ready decomposition of mandelaldehyde, Ph·CH(OH)·CHO, into benzaldehyde and formaldehyde (Rinkes, *Rec. Trav. chim.*, 1920, **39**, 709; Marshall and Walker, *J.*, 1952, 467) and of diphenylglycollaldehyde, $Ph_2C(OH)·CHO$, into benzophenone and formaldehyde (Danilow, *Ber.*, 1927, **60**, 2390; 1929, **62**, 2653; cf. McElvain, Mirviss, and Stevens, *J. Amer. Chem. Soc.*, 1951, **73**, 3807). Alternatively, mesityl oxide may be formed by direct fission of the hydroxy-acid (V), similarly to the decomposition of mandelic acid, $Ph·CH(OH)·CO_2H$, into benzaldehyde and formic acid (Biedermann, *Ber.*, 1886, **19**, 638).

The dimethylacraldehyde, on the other hand, presumably arises through dehydration of the hydroxy-acid (V) to the desired diene acid (VI), followed by hydration of the vinyl grouping in the latter and reversed aldol reaction and decarboxylation of the resulting

isomeric hydroxy-acid (VII). An attempt to prepare the ethyl ester of the acid (V) directly by the action of *iso*butenyl-lithium upon ethyl pyruvate gave a mixture of products which could not be separated satisfactorily.

The methyl ester of the hydroxy-acid (V) proved remarkably resistant to dehydration. Mainly unchanged ester was recovered after heating with potassium hydrogen sulphate or iodine, but dehydration could be effected by naphthalene-2-sulphonic acid at 130—140°. The ultraviolet-light absorption ($\lambda_{max.}$ 2560 Å, ε 11,000) of the product was not incompatible with that expected for the methyl ester of the desired diene acid (VI). However, ozonolysis afforded only a trace of acetone, together with formaldehyde, indicating that rearrangement to the ester of the isomeric diene acid (X) had taken place.

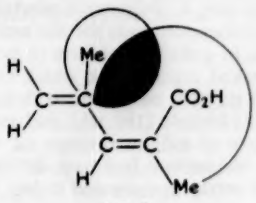
Attempts to dehydrate the methyl ester of (V) under conditions which might be less conducive to isomerisation were unsuccessful; thus treatment with thionyl chloride in pyridine or with phosphoric oxide and triethylamine in benzene (cf. McElvain and Clarke, *J. Amer. Chem. Soc.*, 1947, **69**, 2657) gave mixtures containing unchanged starting material and the methyl ester of (X). Other, more regulated routes to the acid (X) are described below. The formation of the diene-acid (X) from the hydroxy-acid (V) could theoretically proceed along either of two paths, anionotropic rearrangement to the conjugated hydroxy-acid (IX) followed by dehydration, or dehydration to the diene acid (VI), followed by prototropic rearrangement. Acid conditions would normally favour anionotropic rearrangement, but the anionotropic mobility of the acid (V) would, by analogy with 2-hydroxypent-3-enoic acid (Fittig, *Annalen*, 1898, **299**, 37; Braude, *Quart. Rev.*, 1950, **4**, 404), be expected to be low. This makes the path (V) ⟶ (IX) ⟶ (X) less likely, and confirmation was obtained by examining the effect of acid treatment on (V) spectrometrically; the absorption maximum at 2170 Å characteristic of (IX) could not be detected under conditions under which (X) is produced. On the other hand, ethylenic acids and esters are well known to possess high prototropic mobility (Linstead and Noble, *J.*, 1934, 614, and earlier papers) and, although protropy is usually catalysed by bases, acid-catalysed prototropy has been observed to occur in preference to anionotropy in other systems containing strongly electron-attracting substituents (Braude, *loc. cit.*). Thus, the path (V) ⟶ (VI) ⟶ (X) is the more probable one. The apparently ready conversion of (VI) into (X) is not unexpected; although the extent of hyperconjugation in the two isomeric diene-acids will not be very different, the isomer (VI) will be the less stable in virtue of its " cross "-conjugated system, as compared with the " straight "-conjugated system in (X). Thus, the present results suggest that a 1 : 3-diene-2-carboxylic acid system is unlikely to survive unless isomerisation to a 1 : 3-diene-1-carboxylic acid system is structurally precluded.

The hydroxy-aldehyde (IV), like the hydroxy-acid (V), represents a potential anionotropic system, though of a little studied type. The only example analogous to (IV) is the corresponding methyl ketone whose aniontropic mobility was found to be exceptionally low owing to the strong electron-attracting properties of the acetyl group (Braude and Timmons, 1953, *loc. cit.*). With aqueous acids as catalysts, the aldehyde (IV) undergoes rearrangement very much more readily, being converted into the conjugated isomer (VIII) by 2% tartaric acid at room temperature, whereas 2% sulphuric acid at 80° was employed for the ketone. Since a formyl group would be expected, and has in other cases been found, to be ***more*** electron-attracting than an acetyl group (cf. Burkhardt, Horrex, and Jenkins, *J.*, 1936, 1654), the anionotropic mobility of the aldehyde (IV) would be expected to be ***smaller*** than that of the corresponding methyl ketone. It is possible that the reverse relation indicated by the preparative experiments under heterogeneous conditions is only apparent and due to the greater water-solubility of the aldehyde; further discussion of this point is therefore deferred until kinetic data for homogeneous media have been determined.

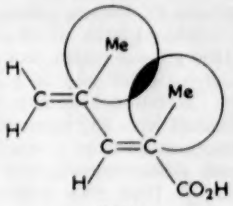
The hydroxy-aldehyde (VIII) showed light absorption typical of the conjugated enal system ($\lambda_{max.}$ 2270 Å). It was characterised by a crystalline 3 : 5-dinitrobenzoate and gave the 2 : 4-dinitrophenylhydrazone of its methyl ether on treatment with methanolic Brady's reagent; the same derivative is obtained from the aldehyde (IV) under these conditions. When either the hydroxy-aldehyde (IV) or the starting acetal (III) was subjected to more

strongly acid conditions, *e.g.*, dilute sulphuric acid, the yields of the rearranged hydroxy-aldehyde (VIII) were much reduced and cyclisation and etherification to give the self-ether of 5-hydroxy-2 : 2 : 4-trimethyl-2 : 5-dihydrofuran (XI) occurred. Analogous changes have been observed with other γ-hydroxy-αβ-ethylenic aldehydes and ketones (Braude and Timmons, 1953, *loc. cit.*). On treatment with 85% phosphoric acid, the ether underwent fission and dehydration to the diene aldehyde (XII) ($\lambda_{max.}$ 2650 Å), characterised by a 2 : 4-dinitrophenylhydrazone ($\lambda_{max.}$ 3950 Å). This diene aldehyde was also obtained by direct pyrolysis of the acetal (III) over aluminium phosphate at 310°. Attempted dehydration of the acetal under milder conditions, *e.g.*, with potassium hydrogen sulphate alumina at 100°, resulted in difficultly separable mixtures of dehydration, hydrolysis, and rearrangement products.

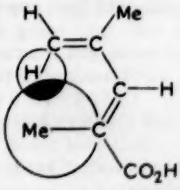
Oxidation of the rearranged hydroxy-aldehyde (VIII) with silver oxide furnished the rearranged hydroxy-acid (IX), which was isolated as the methyl ester after treatment with diazomethane. Dehydration of the ester with naphthalene-2-sulphonic acid gave methyl 2 : 4-dimethylpenta-2 : 4-dienoate, identical in physical properties with that obtained



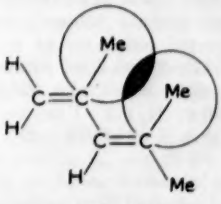
(X*a*)



(X*b*)



(X*c*)



(XIII)

from the hydroxy-acid (V) but giving only formaldehyde on ozonolysis. Alkaline hydrolysis of both samples of ester yielded the free acid as a high-boiling liquid, which gave a crystalline benzylamine salt having an unusual composition in that it contained the acid and amine in the proportion 2 : 1. The ultraviolet and infrared absorption properties of 2 : 4-dimethylpenta-2 : 4-dienoic acid and its methyl ester ($\lambda_{max.}$ 2560 Å, ε 12,500 in ethanol) resemble those of sorbic acid and methyl sorbate ($\lambda_{max.}$ 2580 Å, ε 27,000) as far as the location of the maxima are concerned, but the intensity of the triple chromophore band near 2650 Å is reduced to less than half. This is undoubtedly to be ascribed to the hindrance to uniplanarity in either of the two possible geometrical configurations (X*a*) and (X*b*). Configuration (X*b*), which is the more probable, could adopt either the hindered *s-trans*-conformation shown or the less hindered *s-cis*-conformation (X*c*).* In (X*b*), ε will be reduced relatively to sorbic acid in which the analogous conformation is unhindered, owing to non-planarity of the conjugated system, while in (X*c*) ε will be reduced owing to the decreased effective length of the chromophore (cf. Braude and Waight, " Progress in Stereochemistry," Ed. W. Klyne, Butterworths, London, 1954). The extent of steric overlap in (X*b*) is identical with that in the *s-trans*-conformation of 1 : 1 : 3-trimethylbutadiene (XIII) and it is interesting that the reduction in ε in the hindered diene

* We use the term " configuration " in connexion with geometrical isomerism about conventional double bonds, and the term " conformation " in connexion with rotational isomerism about conventional single bonds in acyclic systems.

($\varepsilon/\varepsilon_0$ = 8500/23,000 = 0·37) is quite similar to that in the hindered diene acid ($\varepsilon/\varepsilon_0$ = 12,500/27,000 = 0·46). The mean interplanar angles θ between the two ethylenic groups in the ground states, calculated from the equation $\cos^2\theta = \varepsilon/\varepsilon_0$ (cf. Braude, Sondheimer, and Forbes, *Nature*, 1954, **173**, 117), are 52° and 47°, respectively.

Experimental

M. p.s were taken on a Kofler block and are corrected. Analytical data were determined by Mr. F. H. Oliver and the staff of the micro-analytical laboratory of this Department. Ultraviolet spectra were determined by Mrs. A. I. Boston using Hilger-Spekker and Unicam instruments. Infrared spectra were determined by R. L. Erskine using a Grubb-Parsons double beam instrument. Microhydrogenations were carried out with platinic oxide in acetic acid.

*iso*Butenyl Bromide.—Bromine (2150 g.) was added dropwise to *tert.*-butyl alcohol (1 kg.), heated under reflux on a steam-bath. After an induction period of a few minutes, the bromine was rapidly decolorised and the rate of addition was adjusted to keep the exothermic reaction under control. After cooling, the top layer (consisting mostly of unchanged alcohol and water) was separated and discarded and the lower layer was washed with water, dried ($CaCl_2$), and distilled once through an 8″ Dufton column, giving 1 : 2-dibromo*iso*butane (2000 g.), b. p. 38—42°/10 mm., n_D^{23} 1·5035—1·5075, which was sufficiently pure for the next stage.

The dibromide (1500 g.) was added dropwise to a stirred mixture of potassium hydroxide (500 g.) in ethylene glycol (1300 ml.) in a 3-necked copper flask which was immersed in an oil-bath at 125—130°. *iso*Butenyl bromide (490 g., 36% based on *tert.*-butyl alcohol) distilled and was collected, washed with 5% potassium hydroxide (100 ml.) and water (3 × 250 ml.), dried ($CaCl_2$), and fractionated from a small piece of sodium through an 8″ Dufton column. It was re-distilled from sodium immediately before use and had b. p. 92°/760 mm., n_D^{24} 1·4615 (Braude and Timmons, *J.*, 1950, 2000, give n_D^{21} 1·4603; Braude and Coles, *J.*, 1950, 2012, give n_D^{23} 1·4610).

Pyruvaldehyde Diethyl Acetal (1 : 1-*Diethoxyacetone*).—Commercial pyruvaldehyde (300 ml.; 30% aqueous solution), ethanol (550 ml.), benzene (550 ml.), and concentrated sulphuric acid were heated under partial reflux for 24 hr., water (330 ml.) being removed azeotropically. The residue was neutralised with solid potassium hydroxide and fractionated, giving the acetal (80 g.) as a very pale yellow liquid; b. p. 52°/11 mm., 47°/7 mm., n_D^{24} 1·4045, $\lambda_{max.}$ 2880 Å, ε 36 in hexane (Found : C, 56·4; H, 9·5. Calc. for $C_7H_{14}O_3$: C, 57·5; H, 9·65%) (Wohl and Lange, *Ber.*, 1908, **41**, 3612, give b. p. 54°/14 mm.; Dakin and Dudley, *J.*, 1914, **105**, 2453, give b. p. 58°/24 mm.).

The corresponding dimethyl acetal, b. p. 40°/10 mm., n_D^{24} 1·4480, was prepared similarly, but in lower yield and admixed with unchanged aldehyde.

1 : 1-*Diethoxy*-2 : 4-*dimethylpent*-3-*en*-2-*ol* (III).—*iso*Butenyl bromide (81 g.) in ether (200 ml.) was added dropwise to a stirred suspension of finely cut lithium (8·3 g.) in ether (800 ml.), under nitrogen. Reaction set in after *ca.* 5 min., and the ether refluxed without external heating. Metallation was complete after 4 hr. Pyruvaldehyde diethyl acetal (45 g.) in ether (100 ml.) was then added and stirring was continued overnight. After cooling to 0°, saturated aqueous ammonium chloride (500 ml.) was added and the ethereal layer was separated, washed with water, dried (Na_2SO_4), and fractionated, giving (i) tetramethylbutadiene (6 g.), b. p. 28°/10 mm., n_D^{22} 1·4662, and (ii) 1 : 1-*diethoxy*-2 : 4-*dimethylpent*-3-*en*-2-*ol* (40 g., 64% based on acetal), b. p. 46°/0·2 mm., n_D^{22} 1·4411 (Found : C, 65·4; H, 11·0. $C_{11}H_{22}O_3$ requires C, 65·3, H, 11·0%). It showed no light absorption with $\varepsilon > 100$ in the 2000—4000 Å range.

The corresponding dimethyl acetal analogous to (III) was obtained under similar conditions in only 10% yield and impure.

No reaction occurred between *iso*butenyl bromide (13·5 g.) and magnesium (2·4 g.) in tetrahydrofuran (200 ml.) even after addition of iodine (20 mg.) and ethyl bromide (0·5 g.) and refluxing for 24 hr. (cf. Normant, *Compt. rend.*, 1954, **239**, 1510; 1955, **240**, 316, 440); practically all the metal was recovered unchanged.

2-*Hydroxy*-2 : 4-*dimethylpent*-3-*en*-1-*al* (IV) *and* 4-*Hydroxy*-2 : 4-*dimethylpent*-2-*en*-1-*al* (VIII).—(*a*) A mixture of the foregoing ethyl acetal (10 g.) and 2% aqueous tartaric acid (200 ml.) was shaken for 14 hr. at 20°. The product was isolated with ether and fractionated, giving 2-*hydroxy*-2 : 4-*dimethylpent*-3-*en*-1-*al* (6 g., 93%), b. p. 80°/11 mm., n_D^{21} 1·4515, $\lambda_{max.}$ 2830 Å, ε 65 in hexane (Found : C, 65·8; H, 9·3. $C_7H_{12}O_2$ requires C, 65·6; H, 9·4%). The 3 : 5-*dinitrobenzoate*, prepared in pyridine–light petroleum, crystallised from light petroleum (b. p. 40—60°) (CO_2–methanol bath) as plates, m. p. 104°, $\lambda_{max.}$ 2280 (ε 23,000) and 2540 Å

(ε 8000) in EtOH (Found: C, 52·5; H, 4·6; N, 8·6. $C_{14}H_{14}O_7N_2$ requires C, 52·2; H, 4·4; N, 8·7%). The aldehyde did not form a semicarbazone under the usual conditions, or a 2 : 4-dinitrophenylhydrazone in boiling pyridine. On treatment with 2 : 4-dinitrophenylhydrazine in methanolic sulphuric acid, the derivative of 4-methoxy-2 : 4-dimethylpent-2-en-1-al (m. p. 160°, undepressed on admixture with the sample described below) was obtained.

(*b*) A mixture of the acetal (10 g.) and 2% aqueous tartaric acid (200 ml.) was shaken for 20 hr. at 20°. Isolation of the products as above and fractionation gave (i) 2-hydroxy-2 : 4-dimethylpent-3-en-1-al (4 g., 62%), b. p. 72°/8 mm., n_D^{23} 1·4502, $\lambda_{max.}$ 2830 Å (ε 65) in hexane (3 : 5-dinitrobenzoate, m. p. 103°, undepressed on admixture with the specimen described above), and (ii) *4-hydroxy-2 : 4-dimethylpent-2-en-1-al* (2 g., 31%), b. p. 102°/10 mm., 61°/0·5 mm., n_D^{26} 1·4651, $\lambda_{max.}$ 2270 Å, ε 9000 in hexane (Found: C, 66·2; H, 9·5. $C_7H_{12}O_2$ requires C, 65·6; H, 9·4%). On treatment with 2 : 4-dinitrophenylhydrazine in methanol–sulphuric acid, the aldehyde gave *4-methoxy-2 : 4-dimethylpent-2-en-1-al* 2 : 4-*dinitrophenylhydrazone* which crystallised from methanol–ethyl acetate in orange needles, m. p. 161°, $\lambda_{max.}$ 3860 Å, ε 28,000 in $CHCl_3$ (Found: C, 52·0; H, 5·7; N, 17·5. $C_{14}H_{18}O_5N_4$ requires C, 52·2; H, 5·6; N, 17·4%).

The proportions of the two aldehydes formed are very sensitive to the conditions. The results of other experiments with aqueous tartaric acid are summarised in the Table; they indicate that the hydrolysis of the acetal to the aldehyde (IV) is faster than the subsequent

Acid concn. (% w/v)	1	2	2	2	2	2	5	6
Time (hr.)	35	14	15·5	17	20	30	20	48
Aldehyde (IV), yield (%) ...	66	93	79	62	62	47	62	45
Aldehyde (VIII), yield (%)	12	<5	16	31	31	35	31	34

rearrangement of the latter to the aldehyde (VIII). In each case, the acetal was shaken with 10—20 ml. of acid at room temperature (20—22°).

(*c*) The acetal (10 g.) and 2% (v/v) sulphuric acid (100 ml.) were shaken together for 24 hr. at 20°. Isolation of the product as above and fractionation gave impure aldehyde (IV) (2·1 g., 34%), b. p. 78—84°/30 mm., n_D^{24} 1·4542, and the aldehyde (VIII) (4·2 g., 68%), b. p. 80—82°/20 mm., n_D^{24} 1·4592.

A similar experiment with 2% (v/v) sulphuric acid for 8 hr. gave 32% of aldehyde (IV) and 16% of aldehyde (VIII), while with 0·2% (v/v) acid for 24 hr. 25% of each aldehyde was obtained.

2 : 4-*Dimethylpenta-2 : 4-dien-1-al* (XII).—(*a*) 1 : 1-Diethoxy-2 : 4-dimethylpent-3-en-2-ol (5 g.) and 4% (v/v) sulphuric acid (200 ml.) were kept at 65° for 26 hr. The products were isolated by extraction with ether and fractionated, giving a mixture of low-boiling materials and then *di-(3 : 5 : 5-trimethyl-2 : 5-dihydro-2-furyl) ether* (?) (XI) (1·6 g.), b. p. 74°/10^{-3} mm., n_D^{24} 1·4778 (Found: C, 70·3; H, 9·35; *M*, in camphor 233. $C_{14}H_{22}O_3$ requires C, 70·55; H, 9·3%; *M*, 238), which gave no precipitate with Brady's reagent in the cold. The ether (XI) was steam-distilled with 85% phosphoric acid (4 ml.), and the distillate (150 ml.) treated with Brady's reagent. The oily derivative formed was extracted with benzene, chromatographed on alumina in benzene–chloroform, and crystallised from ethyl acetate–methanol, giving plates (30 mg.), m. p. 199°, undepressed on admixture with the sample described below.

(*b*) The acetal (III) (4 g.) was passed during 1 hr. through a tube packed with porous tile impregnated with aluminium phosphate at 300—310°/10 mm. (cf. Heilbron, Jones, and Richardson, *J.*, 1949, 287; Leese and Raphael, *J.*, 1950, 2725). The products were collected in a trap at 0° and extracted with ether. The ether extract, which gave a deep colour with Schiff's reagent, was dried (Na_2SO_4) and fractionated, and fractions (2·9 g.) with b. p. 65—75°/10 mm., n_D^{24} 1·4482—1·4488, $\lambda_{max.}$ 2650 Å ($E_{1cm.}^{1\%}$ 250—300) were treated with Brady's reagent, giving 2 : 4-*dimethylpenta-2 : 4-dien-1-al* 2 : 4-*dinitrophenylhydrazone* which after chromatography on alumina in benzene–chloroform crystallised from ethyl acetate–methanol in red plates, m. p. 199°, $\lambda_{max.}$ 3950 Å (ε 32,000 in $CHCl_3$) (Found: N, 19·2. $C_{13}H_{14}O_4N_4$ requires N, 19·3%).

(*c*) The acetal (III) (1·0 g.) was treated with a mixture (0·3 g.) of potassium hydrogen sulphate and alumina for 30 min. at 100°/11 mm. Distillation gave a mixture, b. p. 68—78°/11 mm., n_D^{23} 1·450—1·454, which could not be separated and was treated with Brady's reagent. The resulting red oil was chromatographed, giving: (i) 4-methoxy-2 : 4-dimethylpenta-2 : 4-dien-1-al 2 : 4-dinitrophenylhydrazone, which crystallised from methanol in orange needles, m. p. 161—162°, undepressed on admixture with the sample described above; and (ii) a 2 : 4-*dinitrophenylhydrazone* which crystallised from methanol–ethyl acetate in red needles, m. p. 171°, $\lambda_{max.}$ 3900 Å (ε 25,000 in $CHCl_3$) (Found: C, 53·5; H, 4·8; N, 19·0. $C_{13}H_{14}O_4N_4$ requires C, 53·8;

H, 4·9; N, 19·3%). The latter may be either a stereoisomer of the derivative, m. p. 199°, described above, or possibly the derivative of 4-formyl-2-methylpenta-2 : 4-diene.

Unchanged acetal was recovered from a similar experiment with alumina alone.

2-Hydroxy-2 : 4-dimethylpent-3-enoic Acid (V).—A solution of the aldehyde (IV) (7 g.) and silver nitrate (20 g.) in water (60 ml.) and methanol (50 ml.) was treated dropwise with aqueous 15% potassium hydroxide (100 ml.), with stirring. Stirring was continued for 1 hr. after heat evolution had ceased, the mixture was then made alkaline to phenolphthalein and filtered, and the solution (A) extracted with ether. Evaporation of the ethereal extract (B) and treatment with Brady's reagent gave the 2 : 4-dinitrophenylhydrazone of ββ-dimethylacraldehyde (0·2 g.), which crystallised from ethyl acetate in red needles, m. p. and mixed m. p. 183°, $\lambda_{max.}$ 3860 Å (ε 28,000 in $CHCl_3$) (Found : C, 50·3; H, 4·7; N, 21·0. Calc. for $C_{11}H_{12}O_4N_4$: C, 50·0; H, 4·6; N, 21·2%). The aqueous solution (A) was acidified with hydrochloric acid at 0° and extracted with ether (5 × 50 ml.). The ethereal solution was dried (Na_2SO_4) and treated with a slight excess of diazomethane in ether. The solvent was removed under reduced pressure and the residue was fractionated, giving (i) a mixture (0·6 g.), b. p. 112°/500 mm., of diacetone alcohol and mesityl oxide (2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 202°, $\lambda_{max.}$ 3860 Å, ε 24,000 in $CHCl_3$), and (ii) *methyl 2-hydroxy-2 : 4-dimethylpent-3-enoate* (1·1 g.), b. p. 76—78°/10 mm., 45°/0·3 mm., n_D^{23} 1·4445 (Found : C, 61·1; H, 9·0. $C_8H_{14}O_3$ requires C, 60·7; H, 8·9%). The ester showed no absorption with ε > 100 between 2200 and 4000 Å in ethanol, or after being kept in alcoholic 0·1M-hydrogen chloride for 72 hr. When heated at 80° for 5 hr. the latter solution showed λ_{max} 2580 Å (ε 6500), indicating incomplete dehydration.

4-Hydroxy-2 : 4-dimethylpent-2-enoic Acid (IX).—4-Hydroxy-2 : 4-dimethylpent-2-en-1-al (7 g.) was oxidised with silver oxide, and the products were worked up as above, giving the *methyl ester* (2·5 g.), b. p. 63°/0·2 mm., n_D^{21} 1·4627, $\lambda_{max.}$ 2170 Å (ε 8500 in EtOH) (Found : C, 61·0; H, 9·1. $C_8H_{14}O_3$ requires C, 60·7; H, 8·9%). No aldehydic or ketonic by-products were obtained in this case.

2 : 4-*Dimethylpenta-2 : 4-dienoic Acid* (X).—(*a*) The foregoing methyl ester (1 g.) was heated with naphthalene-2-sulphonic acid (20 mg.) for 10 min. at 130°/100 mm., and then distilled slowly at 10 mm. Redistillation from a trace of naphthalenesulphonic acid gave *methyl* 2 : 4-*dimethylpenta-2 : 4-dienoate* (0·7 g., 79%), b. p. 59°/8 mm., n_D^{23} 1·4758 (Found : C, 68·4; H, 8·7. $C_8H_{12}O_2$ requires C, 68·5; H, 8·6%). Ultraviolet absorption : $\lambda_{max.}$ 2560 (ε 12,500 in EtOH), 2540 Å (ε 11,500 in hexane). Infrared max. (in 0·5% CS_2 solution, 0·05-cm. cell, apparent ε values in parentheses) : 1713 (610, C=O stretching), 1629 (95, C=C stretching), 1274, 1239 (390, 480, C–O stretching), 899, 753 (200, 130, C–H bending), and 1117 cm.$^{-1}$ (420; an unassigned band in this region has been observed in other αβ-ethylenic esters; cf. Bellamy, "The Infrared Spectra of Complex Molecules," Methuen, London, 1954). Methyl sorbate exhibits bands of comparable intensity at 1716, 1642, 1242, 1137, 889, and 796 cm.$^{-1}$. Ozonolysis of the ester (510 mg.) in acetic acid yielded only formaldehyde, isolated as the dimedone derivative (600 mg.), m. p. 189°.

The ester (450 mg.) was treated under reflux with 15% aqueous potassium hydroxide (10 ml.) for 2 hr. under nitrogen. The solution was extracted with ether to remove non-acidic products, acidified with hydrochloric acid, and then extracted again with ether. The ether extract was dried (Na_2SO_4) and evaporated, leaving a gum which could not be crystallised and was distilled, giving the *acid* (200 mg.), b. p. 45—55° (bath-temp.)/10^{-4} mm., n_D^{25} 1·4975, $\lambda_{max.}$ 2540 (ε 11,000 in EtOH), 2460 Å (ε 10,000 in ethanolic 0·1M-potassium hydroxide) (Found : C, 66·5; H, 8·3%; equiv., 134. $C_7H_{10}O_2$ requires C, 66·7; H, 8·0%; *M*, 126. Microhydrogenation no., found 66; required 63).

The *benzylamine salt*, prepared in and crystallised from ethanol, formed needles, m. p. 110°, $\lambda_{max.}$ 2560 Å (ε 22,600 in EtOH) (Found : C, 69·9; H, 8·6; N, 3·9. $2C_7H_{10}O_2,C_7H_9N$ requires C, 70·2; H, 8·1; N, 3·9%).

(*b*) Methyl 2-hydroxy-2 : 4-dimethylpent-3-enoate (3 g.) was dehydrated with naphthalene-2-sulphonic acid as above, giving methyl 2 : 4-dimethyl-2 : 4-pentadienoate (probably admixed with a trace of methyl 4-methylpenta-1 : 3-diene-2-carboxylate) (1·8 g.), b. p. 97°/55 mm., 60°/8 mm., n_D^{28} 1·4715, $\lambda_{max.}$ 2560 (ε 11,500 in EtOH) (Found : C, 68·0; H, 8·6%). The main bands in the infrared spectrum were identical with those reported under (*a*), but there was some additional low-intensity absorption in the 1400—1500 Å region. Ozonolysis of the ester (340 mg.) in acetic acid gave formaldehyde, as the dimedone derivative (430 mg.), m. p. 189°, and a trace of acetone, isolated as the 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 122°. Alkaline hydrolysis of the ester (200 mg.) as above gave 2 : 4-dimethylpenta-2 : 4-dienoic acid (80 mg.), b. p. 45—50° (bath-temp.)/10^{-4} mm., n_D^{21} 1·5018, $\lambda_{max.}$ 2550 Å (ε 11,000 in EtOH)

(Found: C, 66·6; H, 8·3%). The benzylamine salt had m. p. 110°, undepressed on admixture with the specimen obtained as in (*a*).

(*c*) Methyl 2-hydroxy-2 : 4-dimethylpent-3-enoate (1 g.) was added to a mixture of phosphoric oxide (2 g.), triethylamine (2 ml.), and benzene (3 ml.) which was then refluxed for 30 min. (bath-temp. 100—110°) under nitrogen. After cooling, the liquid was decanted and the solid washed with ether (5 ml.). The liquid products and ether extract were combined and fractionated, giving methyl 2 : 4-dimethylpentadienoate, b. p. 83°/17 mm., n_D^{22} 1·4705, $\lambda_{max.}$ 2570 (ε 9000 in EtOH).

Reaction of iso*Butenyl-lithium with Ethyl Pyruvate.*—*iso*Butenyl-lithium (from Li, 4·14 g., and *iso*butenyl bromide, 40·5 g.) in ether (800 ml.) was added to a stirred solution of ethyl pyruvate (11·6 g.) in ether (50 ml.) at 0° under nitrogen. Stirring was continued for 2 hr. at room temp. and saturated aqueous ammonium chloride (300 ml.) was then added. The ether layer was separated, dried (Na_2SO_4–K_2CO_3) and distilled, giving the following main fractions: (i) (4 g.) b. p. 30—35°/11 mm., n_D^{22} 1·467, consisting mainly of tetramethylbutadiene; (ii) (3·5 g.) b. p. 38—40°/10^{-3} mm., n_D^{22} 1·462, $\lambda_{max.}$ 2280 ($E_{1\,cm.}^{1\%}$ 230) and 2560 Å ($E_{1\,cm.}^{1\%}$ 120 in EtOH) (Found: C, 72·85; H, 11·0. Calc. for $C_{12}H_{22}O_2$: C, 72·7; H, 11·2%); (iii) (3·5 g.) b. p. 66—70° (bath-temp.)/10^{-4} mm., n_D^{20} 1·492, $\lambda_{max.}$ 2280 ($E_{1\,cm.}^{1\%}$ 200) and 2560 Å ($E_{1\,cm.}^{1\%}$ 140) (Found: C, 68·0; H, 9·2. Calc. for $C_{12}H_{20}O_3$: C, 67·6; H, 9·4%); and (iv) higher-boiling products, similar in composition and light absorption to (iii). Fraction (iii) was refluxed with aqueous-methanolic potassium hydroxide for 2 hr. and the non-acidic products were isolated with ether, giving a colourless *compound* which after sublimation at 70°/10^{-5} mm. had m. p. 88—90°, $\lambda_{max.}$ 2850 Å ($E_{1\,cm.}^{1\%}$ 80 in EtOH) (Found: C, 65·9; H, 9·1. $C_7H_{12}O_2$ requires C, 65·7; H, 9·3%), and was not further investigated.

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Alkenylation with Lithium Alkenyls. Part X. Some Reactions of Trimethylvinyl-lithium* (1 : 2-*Dimethylpropenyl-lithium*).

By E. A. Braude and E. A. Evans.

[Reprint Order No. 6295.]

The formation of trimethylvinyl-lithium (1 : 2-dimethylpropenyl-lithium) by direct metallation of the bromide, its carboxylation to give αβ-dimethylcrotonic acid, and its reactions with a number of aldehydes and ketones are described.

In previous papers, the formation and reactions of propenyl (2-methylvinyl-) (*J.*, 1951, 2078) and *iso*butenyl-lithium (2 : 2-dimethylvinyl-lithium) (*J.*, 1950, 2007, 2012; 1952, 1425; 1953, 3131; 1955, 3324) have been described. In the meantime, 1-methylpropenyl-lithium (1 : 2-dimethylvinyl-lithium) has been reported by Dreiding and Pratt (*J. Amer. Chem. Soc.*, 1954, **76**, 1902), so that apart from the parent vinyl-lithium, only the 1-methyl and the 1 : 2 : 2-trimethyl derivative are still unknown amongst the methylated vinyl-lithium derivatives. Vinyl-lithium is not formed from either vinyl chloride or vinyl bromide under the usual conditions of direct metallation (unpublished experiments by Dr. K. R. H. Wooldridge) and it is not of great synthetical interest since the desired products are usually accessible through semi-hydrogenation of the corresponding ethynyl compounds obtained from sodium acetylide, and since, moreover, vinylsodium (Morton, Marsh, Coombs, Lyons, Penner, Ramsden, Baker, Little, and Letsinger, *J. Amer. Chem Soc.*, 1950, **72**, 3785) as well as vinylmagnesium halides [Yushchenko, *Zhur. obshchei Khim.*, 1951, **21**, 1244; *Chem. Abs.*, 1952, **46**, 1957; Akiyoshi and Okuno, *J. Chem. Soc. Japan*, 1953, **74**, 467; Normant, *Compt. rend.*, 1954, **239**, 1510, 1811; 1955, **240**, 314, 631] can be utilised. In this paper,

* Part IX, preceding paper.

the formation and some reactions of the fully substituted trimethylvinyl-lithium (1 : 2-dimethylpropenyl-lithium) are detailed.

Trimethylvinyl bromide was conveniently prepared by the direct action of bromine on *tert.*-pentyl alcohol and was readily metallated by metallic lithium in ether. Carboxylation afforded αβ-dimethylcrotonic acid but, in contrast to the corresponding reactions with dimethylvinyl halides, only a small amount of diene formed by a coupling reaction was obtained and there was no trace of ketonic products. αβ-Dimethylcrotonic acid was characterised by a benzylamine salt and exhibits spectral properties typical of an αβ-ethylenic acid (see Table). Progressive alkylation of acrylic acid results in the usual bathochromic displacement of the ultraviolet maxima, as well as in a regular shift of the infrared frequencies associated with C=C and C=O stretching vibrations, which can be interpreted as arising from a decrease in the strength of the C=C and C=O bonds, due to the increasing importance of resonance of the type C=C–C=O ⟷ C^+–C=C–O^-. A simultaneous decrease in the intensities of the ultraviolet bands may be associated with weak steric interference between the carboxyl and *cis*-β-methyl groups (cf. Braude and Waight in "Progress in Stereochemistry," ed. W. Klyne, Vol. I, Chapter 4, Butterworths, London, 1954; Part IX, *J.*, 1955, 3324), but since the ε values for the lower homologues are not very accurate (cf. Ungnade and Ortega, *J. Amer. Chem. Soc.*, 1951, **73**, 1564; 1952, **74**, 6313; Jones, Whitham, and Whiting, *J.*, 1954, 1865) detailed consideration of these data is deferred.

Trimethylvinyl-lithium reacted normally with the following aldehydes and ketones, giving the secondary or tertiary allylic alcohols in good to moderate yields: from acraldehyde, (I; R = CH:CH_2; 27%); from crotonaldehyde, (I; R = CH:CHMe; 29%); from benzaldehyde, (I; R = Ph; 41%); from mesityl oxide, (II; R = CH:CMe_2; 67%); from acetophenone, (II; R = Ph; 36%); and from benzophenone, (III; 56%). The structures of the products were confirmed by their spectral properties and by micro-hydrogenation. The secondary alcohols obtained from acraldehyde and crotonaldehyde were also oxidised by chromium trioxide to the diethylenic ketones (IV; R = H and Me). Other reactions of the alcohols will be described later.

(I) CMe_2:CMe·CHR·OH CMe_2:CMe·CMeR·OH (II)

(III) CMe_2:CMe·CPh_2·OH CMe_2:CMe·COR (IV)

Light absorption of αβ-ethylenic acids.

	Ultraviolet *		Infrared †			Ultraviolet *		Infrared †	
	$\lambda_{max.}$ (Å)	ε	$\nu_{C=O}$	$\nu_{C=C}$		$\lambda_{max.}$ (Å)	ε	$\nu_{C=O}$	$\nu_{C=C}$
CH_2:CH·CO_2H ...	<2100	— [1]	1705	?	CHMe:CMe·CO_2H	2155	9400 [4]	1689	1645
CH_2:CMe·CO_2H ...	<2100	—	1700	?	CMe_2:CH·CO_2H ...	2160	12,000 [5]	1689	1637
CHMe:CH·CO_2H	2060	15,000 [2]	1698	1653	CMe_2:CMe·CO_2H ...	2210	9700 [5]	1675	1621
CHMe:CMe·CO_2H	2125	12,500 [3]	1684	1647					

* In ethanol. † Stretching frequencies in $cm.^{-1}$ (paraffin mulls).
[1] Ungnade and Ortega, *loc. cit.* [2] *trans*-Crotonic acid (measurement by Dr. C. J. Timmons). [3] Tiglic acid (Dreiding and Pratt, *loc. cit.*). [4] Angelic acid (*idem, loc. cit.*). [5] This paper. [6] Flett, *J.*, 1951, 962.

Experimental

For general methods, see Part IX, *loc. cit.*

1 : 2-*Dimethylpropenyl Bromide.*—Bromine (1 kg.) was added dropwise to *tert.*-pentyl alcohol (550 g.) which was heated under reflux on the steam-bath. There was immediate decolorisation and the alcohol refluxed vigorously. When all the bromine had been added, the mixture was allowed to cool. The lower dibromide layer was separated, washed with water (3 × 250 ml.), and dried ($CaCl_2$). Distillation through an 8″ Dufton column gave a fraction (645 g.) of 2 : 3-dibromo-3-methylbutane, b. p. 58—63°/14 mm., n_D^{24} 1·5001 [Pansevich-Kolyada and Prilezhaev, *Zhur. obshchei Khim.*, 1951, **21**, 517, give b. p. 56—58°/12 mm., n_D^{20} 1·5112], which was sufficiently pure for the next stage.

The dibromide (645 g.) was added dropwise with vigorous stirring to potassium hydroxide (250 g.) in ethylene glycol (800 ml.) in a three-necked copper flask at 165—170° and the alkenyl

bromide was allowed to distil as it was formed. The distillate was washed with 5% aqueous potassium hydroxide (100 ml.) and water (4 × 250 ml.), dried ($CaCl_2$), and fractionated through an 8" Dufton column from a small piece of sodium, giving 1 : 2-dimethylpropenyl bromide (115 g., 12% overall yield from *tert.*-pentyl alcohol), b. p. 120—121°/750 mm., n_D^{23} 1·4700 (Farrell and Bachman, *J. Amer. Chem. Soc.*, 1935, **57**, 1281, give b. p. 118—120°, n_D^{20} 1·4738).

αβ-*Dimethylcrotonic Acid.*—The foregoing bromide (10 g.) was added to a well-stirred suspension of finely-cut lithium (1 g.) in anhydrous ether (200 ml.) under nitrogen. Reaction set in after a few minutes and metallation was complete after 2—3 hr. under reflux. The green-grey mixture was cooled, added to powdered carbon dioxide (300 g.), and allowed to attain room temperature. Water (100 ml.) was then added and the solution acidified dropwise with concentrated hydrochloric acid. The ether layer was separated, extracted with 2N-sodium carbonate (2 × 100 ml.), dried (Na_2SO_4), and evaporated, giving a small amount of neutral products (0·3 g.) which showed no absorption with $E^{1\%}_{1\,cm.}$ >50 between 2200 and 4000 Å and gave no 2 : 4-dinitrophenylhydrazone, but rapidly decolorised a solution of bromine in carbon tetrachloride. This was probably impure 2 : 3 : 4 : 5-tetramethylhexa-2 : 4-diene, which, like hexachlorobutadiene (cf. Szasz and Sheppard, *Trans. Faraday Soc.*, 1953, **49**, 358; Braude and Waight, *loc. cit.*), would not be expected to show a typical diene band, owing to steric hindrance. Microfractionation gave a middle cut, b. p. 80°/20 mm., n_D^{20} 1·4485 (Found: C, 86·4; H, 12·4. $C_{10}H_{18}$ requires C, 87·0; H, 13·0%. Hydrogenation no., 106. Calc. for 2 double bonds, 69). The sodium carbonate extract was acidified at 0° with concentrated hydrochloric acid and extracted with ether. The ethereal solution was dried (Na_2SO_4) and evaporated, and the residue crystallised from light petroleum (b. p. 40—60°), giving αβ-dimethylcrotonic acid (1·8 g., 17%), m. p. 70—71°, $\lambda_{max.}$ 2210 Å, ε 9700 in EtOH (Found: C, 63·4; H, 9·0. Calc. for $C_6H_{10}O_2$: C, 63·1; H, 8·8%) (Gakhokidze, *Zhur. obshchei Khim.*, 1947, **17**, 1327, and Hauser *et al.*, *J. Amer. Chem. Soc.*, 1953, **75**, 1068, give m. p. 70—71°]. The *benzylamine salt* crystallised from ethyl acetate in needles, m. p. 106—107° (Found: C, 70·9; H, 8·6; N, 6·35. $C_{13}H_{19}O_2N$ requires C, 70·6; H, 8·6; N, 6·3%).

2 : 3-*Dimethylhexa*-2 : 5-*dien*-4-*ol.*—Acraldehyde (4 g.) in anhydrous ether (25 ml.) was added to 1 : 2-dimethylpropenyl-lithium (from lithium, 1 g., and the bromide, 10 g.) in ether (170 ml.) at 10°. The mixture was stirred for 1 hr. at room temperature and ice-cold saturated aqueous ammonium chloride (150 ml.) was then added. The ether layer was separated, dried (Na_2SO_4–K_2CO_3), and fractionated from a trace of potassium carbonate, giving 2 : 3-*dimethylhexa*-2 : 5-*dien*-4-*ol* (2·3 g., 27%), b. p. 75—76°/10 mm., n_D^{23} 1·4702, ε <500 between 2100 and 4000 Å (Found: C, 75·9; H, 11·4. $C_8H_{14}O$ requires C, 76·1; H, 11·2%. Hydrogenation no. 53. Calc. for 2 double bonds, 63).

The dienol (0·6 g.) in dry pyridine (6 ml.) was added to chromium trioxide (0·6 g.) in pyridine (6 ml.). The mixture was kept for 3 days at room temperature and then added to water (100 ml.). The solution was extracted with ether, and the ether extract was dried (Na_2SO_4) and evaporated under reduced pressure. Treatment of the residue with 2 : 4-dinitrophenylhydrazine in methanol–sulphuric acid gave 2 : 3-*dimethylhexa*-2 : 5-*dien*-4-*one* 2 : 4-*dinitrophenylhydrazone* (0·2 g.) which crystallised from ethyl acetate–methanol in dark red needles, m. p. 225—226°, $\lambda_{max.}$ 3970 Å (ε 30,000 in $CHCl_3$) (Found: C, 54·5; H, 5·6; N, 18·5. $C_{14}H_{18}O_4N_4$ requires C, 55·3; H, 5·3; N, 18·4%).

2 : 3-*Dimethylhepta*-2 : 5-*dien*-1-*ol.*—Crotonaldehyde (5 g.) in anhydrous ether (25 ml.) was added to a solution of 1 : 2-dimethylpropenyl-lithium (from lithium, 1 g., and bromide, 10 g.), in ether (170 ml.) at 0°. The solution was stirred for 2 hr. at room temperature. Isolation of the products as above gave 2 : 3-*dimethylhepta*-2 : 5-*dien*-4-*ol* (2·7 g., 29%), b. p. 60—61°/1 mm., n_D^{24} 1·4758, ε <500 between 2100 and 4000 Å (Found: C, 76·7; H, 11·5. $C_9H_{16}O$ requires C, 77·1; H, 11·5%. Hydrogenation no., 69. Calc. for 2 double bonds, 70). The dienol was very unstable and decomposed even at 0°.

The dienol (0·6 g.), oxidised as above, gave, after treatment with Brady's reagent, 2 : 3-*dimethylhepta*-2 : 5-*dien*-4-*one* 2 : 4-*dinitrophenylhydrazone* (0·2 g.) which crystallised from ethyl acetate–methanol in red plates, m. p. 215—216°, $\lambda_{max.}$ 3980 Å (ε 32,000 in $CHCl_3$) (Found: C, 56·2; H, 6·2; N, 17·7. $C_{15}H_{18}O_4N_4$ requires C, 56·6; H, 5·7; N, 17·6%).

2 : 3 : 4 : 6-*Tetramethylhepta*-2 : 5-*dien*-4-*ol.*—Mesityl oxide (14 g.) in anhydrous ether (25 ml.) with 1 : 2-dimethylpropenyl-lithium (from lithium, 3·3 g., and bromide, 25 g.) in ether (350 ml.) gave, as above, 2 : 3 : 4 : 6-*tetramethylhepta*-2 : 5-*dien*-4-*ol* (16 g., 67%), b. p. 45°/0·1 mm., n_D^{23} 1·4720, ε <1000 between 2100 and 4000 Å (Found: C, 78·4; H, 12·1. $C_{11}H_{20}O$ requires C, 78·5; H, 12·0%).

2 : 3-*Dimethyl*-1-*phenylbut*-2-*en*-1-*ol.*—Benzaldehyde (7 g.) in anhydrous ether (25 ml.)

with 1 : 2-dimethylpropenyl-lithium (from metal, 1 g., and bromide, 12 g.) gave, as above, the *alcohol* (5·8 g., 41%), b. p. 125° (bath-temp.)/10^{-5} mm., n_D^{20} 1·5370 (Found : C, 81·5; H, 9·25. $C_{12}H_{16}O$ requires C, 81·8; H, 9·15%. Hydrogenation no., 42. Calc. for 4 double bonds, 44).

3 : 4-*Dimethyl*-2-*phenylpent*-3-*en*-2-*ol*.—Acetophenone (14 g.) in anhydrous ether (50 ml.) was added dropwise to a solution of 1 : 2-dimethylpropenyl-lithium (from metal, 2 g., and bromide, 20 g.), in ether (300 ml.). The solution was stirred for 1 hour at room temperature. Isolation as above gave the *alcohol* (8 g., 36%), b. p. 53° (bath-temp.)/10^{-5} mm., n_D^{23} 1·5300 (Found : C, 82·0; H, 9·5. $C_{13}H_{18}O$ requires C, 82·1; H, 9·5%).

2 : 3-*Dimethyl*-1 : 1-*diphenylbut*-2-*en*-1-*ol*.—Benzophenone (8·6 g.) in anhydrous ether (25 ml.) was added to 1 : 2-dimethylpropenyl-lithium (from metal, 0·8 g., and bromide, 8 g.) in ether (170 ml.), and the solution was stirred for 30 min. at room temperature. Working up as above gave the *alcohol* (7·5 g., 56%), b. p. 68° (bath-temp.)/5 × 10^{-5} mm., n_D^{25} 1·5949 (Found : C, 85·6; H, 7·7. $C_{16}H_{20}O$ requires C, 85·7; H, 8·0%).

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Alkenylation with Lithium Alkenyls. Part XI. A New Synthesis of Ethylenic Aldehydes.*

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Lithium alkenyls with dimethylformamide give ethylenic aldehydes in moderate yields. In this way, 3-methyl- and 2 : 3-dimethyl-crotonaldehyde, 1-formyl*cyclo*hexene, and 1-formyl*cyclo*heptene have been prepared. The reaction with *cis*-propenyl-lithium gave a mixture from which neither *cis*- nor *trans*-crotonaldehyde could be isolated.

In previous parts of this series, the reactions of lithium alkenyls with aldehydes and ketones to give ethylenic alcohols, and with carboxylic acid derivatives to give ethylenic ketones, have been explored. In this paper the use of lithium alkenyls for the synthesis of ethylenic aldehydes is described.

A variety of reagents have been employed for the conversion of Grignard reagents and organic lithium compounds into aldehydes. The most common of these is ethyl orthoformate, but it was previously reported (Braude and Coles, Part III, *J.*, **1950**, 2012) that no reaction can be effected with *iso*butenyl-lithium under the usual conditions and a negative result has now been obtained with trimethylvinyl-lithium. *N*-substituted formamides have been less widely used as formylating agents, but Sicé (*J. Amer. Chem. Soc.*, **1953**, **75**, 3697; *J. Org. Chem.*, **1954**, **19**, 70) has recently described the conversion of thienyl-lithium into 1-thenaldehyde by *N*-dimethylformamide. This amide, which is available commercially, was also found to react with lithium alkenyls to give the expected aldehydes. Although the yields are only moderate, the method is of practical value.

$$RLi + NMe_2{\cdot}CHO \longrightarrow NMe_2{\cdot}CHR{\cdot}OLi \longrightarrow R{\cdot}CHO + NHMe_2$$

In the case of *iso*butenyl-lithium which yields 3-methylcrotonaldehyde (I) (see Table), a compound accessible by a variety of other routes (*inter al.*, Fischer and Löwenberg, *Annalen*, **1932**, **494**, 233; Young and Linden, *J. Amer. Chem. Soc.*, **1947**, **69**, 2912; Wendler and Slates, *ibid.*, **1950**, **72**, 5341), the product is contaminated with 4-formyl-3-hydroxy-1 : 5 : 5-trimethyl*cyclo*hexene (a dimer known to be formed from the aldehyde under basic conditions) and its dehydration product, 4-formyl-1 : 5 : 5-trimethyl*cyclo*hexa-1 : 3-diene (Fischer and Löwenberg, *loc. cit.*). Trimethylvinyl-lithium afforded 2 : 3-dimethylcrotonaldehyde (II), which was characterised as the semicarbazone and 2 : 4-dinitrophenylhydrazone, both exhibiting the expected light absorption properties. The preparation of this aldehyde was claimed by Prévost (*Bull. Soc. chim. France*, **1944**, **11**, 218), but the

* Part X, preceding paper.

melting point of the semicarbazone recorded by him is different from that obtained here. No aldehyde dimer was encountered in this case.

The reaction of dimethylformamide with *cyclo*hexenyl-lithium gave 1-formyl*cyclo*hexene (III) the properties of which were in excellent agreement with those previously recorded (Plattner and Jampolsky, *Helv. Chim. Acta*, 1943, **26**, 687; Heilbron *et al.*, *J.*, 1949, **737**; Seifert and Schinz, *Helv. Chim. Acta*, 1951, **34**, 728). *cyclo*Heptenyl-lithium similarly furnished 1-formyl*cyclo*heptene (IV) which exhibited light-absorption properties almost identical with those of the lower homologue and gave a semicarbazone (m. p. 211°) and a 2 : 4-dinitrophenylhydrazone. This aldehyde was first prepared by Wallach and Köhler (*Annalen*, 1906, **345**, 152) from methylene*cyclo*heptane, though only isolated as the semicarbazone (m. p. 203°).

Unlike the other lithium alkenyls, *cis*-propenyl-lithium failed to give the corresponding aldehyde. This case was of particular interest, since *cis*-crotonaldehyde, which appears to be isomerised to the *trans*-isomer with great ease and has never been isolated, might possibly have survived under the present (basic) reaction conditions (cf. Raphael and Sondheimer, *J.*, 1951, 2693, Schinz and his co-workers, *Helv. Chim. Acta*, 1955, **38**, 239, 255). However, only higher-boiling products could be isolated; some of these gave crystalline carbonyl derivatives but were not further investigated.

The ultraviolet-light absorption properties of the above ethylenic aldehydes and their derivatives (see Table) mostly conform to well-known generalisations (cf. Evans and Gillam, *J.*, 1943, 565; Braude and Jones, *J.*, 1945, 498), but certain minor anomalies are apparent, particularly in the short-wavelength bands of the aldehydes. The low ultraviolet absorption intensity exhibited by 3-methylcrotonaldehyde suggested that it might be a mixture of the conjugated and the unconjugated isomer (3-methylbut-3-en-1-al), as observed for mesityl oxide (Gray, Rasmussen, and Tunnicliff, *J. Amer. Chem. Soc.*, 1947, **69**, 1630) and a number of related ethylenic ketones (Braude, Jones, Koch, Sondheimer, and Toogood, *J.*, 1949, 1890), but the infrared spectrum showed no bands expected for an isolated $>C=O$ or $>C=CH_2$ group.

Ultraviolet-light absorption of some ethylenic aldehydes and their derivatives.

	Aldehyde [1]		Semicarbazone [2]		2 : 4-Dinitrophenylhydrazone [3]	
	$\lambda_{max.}$ (Å)	ε	$\lambda_{max.}$ (Å)	ε	$\lambda_{max.}$ (Å)	ε
$CH_2{:}CH{\cdot}CHO$	2080	>10,000 [a]	2640	19,000	3660	25,500 [c]
	3280	13				
$CHMe{:}CH{\cdot}CHO$ ...	2170	16,000	2645	24,000	3720	29,000 [c]
	3210	20				
(I) $CMe_2{:}CH{\cdot}CHO$	2300	6500	2700	28,000	3810	30,000
(II) $CMe_2{:}CMe{\cdot}CHO$ ...	2390	13,500	2710	27,000	3860	27,000
	2370	12,000 [b]	2670	30,500 [b]	3770	29,500 [b]
(III)	2270	11,000	2660	26,000	3810	27,600
	3200	22				
(IV)	2280	12,000	2680	27,000	3810	29,000
	3200	24				

[1] In hexane. [2] In ethanol. [3] In chloroform.

[a] Evans and Gillam, *J.*, 1943, 565. [b] Heilbron, Jones, Toogood, and Weedon, *J.*, 1949, 1827. [c] Braude and Jones, *J.*, 1945, 498.

Experimental

For general methods, see Part IX, *J.*, 1955, 3324. Spectral data are given only when not included in the Table.

3-*Methylcrotonaldehyde*.—Dimethylformamide (7·3 g.) in anhydrous ether (25 ml.) was added to *iso*butenyl-lithium (from metal, 1·5 g., and *iso*butenyl bromide, 13·5 g., see Part IX, *loc. cit.*) in ether (250 ml.) at room temperature. The solution was then refluxed for 30 min. and, after being stirred at room temperature overnight, was treated with excess of saturated aqueous ammonium chloride at 0°. The ethereal layer was separated, dried (Na_2SO_4), and fractionated through an 8″ Dufton column, giving (i) 3-methylcrotonaldehyde (2·3 g., 27%), b. p. 30—32°/

12 mm., $\nu_{max.}$ (liquid film) 1682 (s, C=O stretching) and 835 (s, C–H bending in $R_2C{:}CHR$), no bands near 1710 and 890 cm.$^{-1}$, identified as the semicarbazone, m. p. and mixed m. p. 213° (from methanol), and as the 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 183° (from ethyl acetate) (Found : N, 21·1. Calc. for $C_{11}H_{12}O_4N_4$: N, 21·2%), (ii) the dimer (2 g., 12%), b. p. 113°/20 mm., which was dehydrated by distillation from a trace of naphthalene-2-sulphonic acid to give slightly impure 4-formyl-1 : 1 : 5-trimethyl*cyclo*hexa-1 : 3-diene, b. p. 102°/18 mm., n_D^{22} 1·5175, $\lambda_{max.}$ 3080 Å (ε 9000 in hexane) (Found : C, 79·4; H, 10·0. Calc. for $C_{10}H_{14}O$: C, 79·95; H, 9·4%) (Fischer and Löwenberg, *Annalen*, 1932, **494**, 263, give b. p. 85°/9 mm., n_D^{20} 1·5267), which formed a semicarbazone, m. p. 209° (from methanol), $\lambda_{max.}$ 3220 Å (ε 20,000 in EtOH) (Fischer and Löwenberg, *loc. cit.*, give m. p. 213°). Both the dimer and its dehydration product furnished 4-formyl-1 : 5 : 5-trimethyl*cyclo*hexadiene-2 : 4-dinitrophenylhydrazone, m. p. 204° (from ethyl acetate–methanol), $\lambda_{max.}$ 4080 Å (ε 30,500 in $CHCl_3$), identical with a specimen prepared by Dr. E. S. Waight.

2 : 3-*Dimethylcrotonaldehyde*.—Dimethylformamide (9 g.) in ether (50 ml.) was added to a solution of 1 : 2-dimethylpropenyl-lithium (from lithium, 2·0 g., and bromide, 20 g.; cf. Part X, *loc. cit.*) in ether (300 ml.) at room temperature. The mixture was stirred for 2 hr. at room temperature and saturated ammonium chloride (300 ml.) was then added. The ethereal layer was separated, dried (Na_2SO_4), and distilled, giving the aldehyde (5·5 g., 40%), b. p. 42—43°/9 mm., n_D^{19} 1·4702, $\lambda_{max.}$ 2830 Å (ε 11,800 in hexane) (Found : C, 73·4; H, 10·5. Calc. for $C_6H_{10}O$: C, 73·4; H, 10·3%) (Prévost, *Bull. Soc. chim. France*, 1944, **11**, 218, gives b. p. 81°/65 mm., n_D^{23} 1·4686). This was converted into the *semicarbazone* which crystallised from methanol in plates, m. p. 239—240° (Found : C, 54·4; H, 8·6; N, 27·2. $C_7H_{13}ON_3$ requires C, 54·2; H, 8·4; N, 27·1%) (Prévost, *loc. cit.*, gives m. p. 276°). Steam-distillation of a mixture of the semicarbazone (8 g.) and phthalic anhydride (12 g.) in water (140 ml.) gave 2 : 3-dimethylcrotonaldehyde (3·5 g., 69%) which on redistillation had b. p. 41°/8 mm., n_D^{18} 1·4704. The 2 : 4-*dinitrophenylhydrazone* crystallised from ethyl acetate in red needles, m. p. 200—201° (Found : 52·1; H, 5·1; N, 20·6. $C_{12}H_{14}O_4N_4$ requires C, 51·8; H, 5·1; N, 20·1%).

1-*Formyl*cyclo*hexene*.—Dimethylformamide (10 g.) in ether (30 ml.) was added to *cyclo*hexenyl-lithium (from metal, 2·3 g., and 1-chloro*cyclo*hexene, 15 g.; cf. Braude and Coles, *J.*, 1950, 2014) in ether (200 ml.) at room temperature. The mixture was stirred for 30 min. and then treated with excess of saturated ammonium chloride solution. Isolation of the product as above and fractionation gave 1-formyl*cyclo*hexene (3·5 g., 26%), b. p. 72°/15 mm., n_D^{23} 1·4920 (Seifert and Schinz, *Helv. Chim. Acta*, 1951, **34**, 728, give b. p. 60—61°/11 mm., n_D^{19} 1·4914). It was identified as the semicarbazone, m. p. 217—218° (from methanol) (Plattner and Jampolsky, *ibid.*, 1943, **26**, 687, give m. p. 213—216°; Heilbron *et al.*, *J.*, 1949, 737, give m. p. 213—214°), and as the 2 : 4-dinitrophenylhydrazone, m. p. 223—224° (from ethyl acetate) (Found : C, 53·7; H, 4·9; N, 19·8. Calc. for $C_{13}H_{14}O_4N_4$: C, 53·8; H, 4·9; N, 19·3%) (Heilbron, *et al.*, *loc. cit.*, give m. p. 219—220°; Seifert and Schinz, *Helv. Chim. Acta*, 1951, **34**, 728, give m. p. 212°).

1-*Formyl*cyclo*heptene*.—Dimethylformamide (35 g.) in ether (100 ml.) was added to *cyclo*heptenyl-lithium (from metal, 9 g., and 1-chloro*cyclo*heptene, 70 g.; cf. Braude, Forbes, and Evans, *J.*, 1953, 2202) in ether (1 l.). After being stirred for 2 hr., the mixture was treated with excess of saturated ammonium chloride, and the products were isolated as above. Fractionation gave 1-*formyl*cyclo*heptene* (37 g., 70%), b. p. 82—83°/9 mm., n_D^{20} 1·4983 (Found : C, 77·7; H, 9·95. $C_8H_{12}O$ requires C, 77·45; H, 9·7%). The semicarbazone crystallised from methanol in plates, m. p. 210—211° (Found : C, 59·7; H, 8·5; N, 23·6. Calc. for $C_9H_{15}ON_3$: C, 59·6; H, 8·3; N, 23·2%) (Wallach and Köhler, *Annalen*, 1906, **345**, 152, give m. p. 203—204°). The 2 : 4-*dinitrophenylhydrazone* crystallised from ethyl acetate in red needles, m. p. 210—211° (Found : C, 54·9; H, 5·4; N, 19·7. $C_{14}H_{16}O_4N_4$ requires C, 55·25; H, 5·3; N, 18·4%). Microhydrogenation of the aldehyde in glacial acetic acid–platinum oxide resulted in the uptake of 0·9 mol. of hydrogen.

α-(cyclo*Hept*-1-*enyl*)*benzyl Alcohol*.—The foregoing aldehyde (3·5 g.) in ether (25 ml.) was added to a stirred solution of phenylmagnesium bromide (from magnesium, 0·8 g., and bromobenzene, 5·3 g.) in ether (75 ml.). After 4 hr. excess of aqueous ammonium chloride was added and the ethereal layer was separated, dried (Na_2SO_4–K_2CO_3), and fractionated from a trace of potassium carbonate, giving the alcohol (3·5 g., 61%), b. p. 73° (bath-temp.)/10^{-4} mm., n_D^{25} 1·5521, ε <1000 between 2000 and 4000 Å (Found : C, 82·9; H, 9·15. Calc. for $C_{14}H_{18}O$: C, 83·1; H, 9·0%) (Braude and Forbes give b. p. 94°/0·002 mm., n_D^{24} 1·5429, for a sample prepared from *cyclo*heptenyl-lithium and benzaldehyde and probably contaminated with hydrobenzoin).

Reaction of cis-*Propenyl-lithium with Dimethylformamide*.—The amide (11 g.) in ether (25 ml.) was added to a stirred solution of *cis*-propenyl-lithium (from metal, 2·1 g., and 1-bromopropene,

18 g.; cf. Braude and Coles, *J.*, 1951, 2078) in ether (600 ml.) at 0°. The solution was allowed to attain room temperature (*ca.* 1 hr.), cooled again to 0°, and treated with saturated aqueous ammonium chloride (250 ml.). The ethereal layer was separated, dried (Na_2SO_4), and fractionated, giving a range of fractions (total 1·6 g.), b. p. 80°/90 mm. to 60°/17 mm., n_D^{22} 1·428—1·462. The middle fractions gave strong positive Schiff's tests and afforded a *semicarbazone* which crystallised from aqueous methanol in plates, m. p. 211—213°, $\lambda_{max.}$ 2950 Å ($E_{1cm.}^{1\%}$ 1750 in EtOH) (Found: C, 55·8; H, 7·7; N, 25·7. $C_8H_{13}ON_3$ requires C, 57·5; H, 7·8; N, 25·1%), and a 2 : 4-*dinitrophenylhydrazone* which crystallised from ethyl acetate–methanol in crimson needles, m. p. 204—205°, $\lambda_{max.}$ 3920 Å ($E_{1cm.}^{1\%}$ 1040 in $CHCl_3$) (Found: C, 54·0; H, 5·1; N, 19·9. $C_{13}H_{14}O_4N_4$ requires C, 53·8; H, 4·9; N, 19·3%). The analytical and spectral data suggest that these are the derivatives of a conjugated diene-aldehyde $C_7H_{10}O$, possibly hepta-2 : 4-dien-1-al.

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Alkenylation with Lithium Alkenyls. Part XII. Dihydronaphthyl and Indenyl Derivatives.*

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4- and 3-Chloro-1 : 2-dihydronaphthalene, prepared from α- and β-tetralone, respectively, have been converted by direct metallation into 3 : 4-dihydro-1- and -2-naphthyl-lithium and thence into 3 : 4-dihydro-1- and -2-naphthoic acid.

3-Chloroindene failed to react with lithium, while 2-chloroindene underwent metallation at the $-CH_2-$ rather than at the $=CCl-$ group, as shown by the formation of 2-chloroindene-3-carboxylic acid on carboxylation.

Since it has been shown that lithium alkenyls can readily be obtained from 1-chloro*cyclo*alkenes (Braude and Coles, *J.*, 1950, 2014; Braude and Forbes, *J.*, 1951, 1755, and later papers) as well as from 2-arylated vinyl halides (Wright, *J. Org. Chem.*, 1936, **1**, 457), it might be expected that the same would be true of derivatives combining these structural features. Dihydronaphthyl-lithium and similar derivatives are of interest as possible synthetical reagents in the field of hydroaromatic systems and in the present paper a study of their formation and stability is reported.

α-Tetralone, which is most conveniently prepared by the oxidation of tetralin with chromic acid [Nazarov and Burmistrova, *Zhur. obshchei Khim.*, 1950, **20**, 1304], was converted by phosphorus pentachloride into a mixture of 3-chloro-1 : 2-dihydronaphthalene (II) and 1 : 1-dichlorotetralin, which are readily separated by fractionation. The ethylenic chloride was attacked slowly by lithium in refluxing ether, about 60 hours being required for complete reaction. Carboxylation furnished 3 : 4-dihydro-1-naphthoic acid (IV; see Table) (12%), together with polymeric products, possibly formed through self-addition or exchange metallation of the lithium alkenyl. The acid has previously been prepared by other methods (Baeyer, *Annalen*, 1891, **266**, 169, 175; Kay and Morton, *J.*, 1914, **105**, 1574; Fieser and Holmes, *J. Amer. Chem. Soc.*, 1936, **58**, 2319): it was characterised as a benzylamine salt. On dehydrogenation with palladium–charcoal at 290°, it gave mainly naphthalene (68%), in contrast to dehydrogenation with sulphur at 230° which yields mainly 1-naphthoic acid (Fieser, Fieser, Hershberg, Holmes, and Newman, *Science*, 1936, **83**, 558). Attempted formylation of 3 : 4-dihydro-1-naphthyl-lithium with dimethylformamide (Part XI, *loc. cit.*) yielded a mixture from which only a small amount of a 2 : 4-dinitrophenylhydrazone, corresponding to the hydrate of the derivative of 3 : 4-dihydro-1-naphthaldehyde, could be isolated.

3-Chloro-1 : 2-dihydronaphthalene (III), similarly prepared from β-tetralone, was

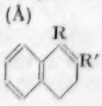
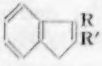
* Part XI, preceding paper.

metallated somewhat more rapidly (24 hours) than the 4-chloro-derivative; in both cases, the reaction was accompanied by an intense red coloration previously observed only with alkadienyl-lithium derivatives (Part VIII, Braude and Evans, *J.*, 1954, 607). Carboxylation gave 3 : 4-dihydro-2-naphthoic acid (V) (8%), again accompanied by polymeric material from which it was separated by sublimation in a high vacuum. The acid was characterised by a benzylamine salt which contained two molar proportions of acid to one of amine, a phenomenon previously encountered with 2 : 4-dimethylpentadienoic acid (Part IX, Braude and Evans, *J.*, 1955, 3324); it is presumably a freak of crystal lattice structure rather than a chemical effect.

3-Chloroindene (VII) prepared from indan-1-one (cf. Braun and Ostermayer, *Ber.*, 1937, **70**, 1006) was not appreciably attacked by lithium in refluxing ether after 50 hours. 2-Chloroindene (VIII), prepared by dehydrochlorination of 1 : 2-dichloroindane (Suter and Lutz, *J. Amer. Chem. Soc.*, 1938, **60**, 1360), reacted very slowly, over 110 hours being required for complete consumption of the metal. Carboxylation gave a chloro-carboxylic acid, which was characterised as the methyl ester and from its ultraviolet-light absorption (see below) is formulated as 2-chloroindene-3-carboxylic acid (IX). The $-CH_2-$ group in 2-chloroindene is evidently more reactive towards metallation than the $=CCl-$ group, and carboxylation appears to be accompanied by a migration of the double bond into the most highly conjugated position.

Light-absorption Data.—Ultraviolet-absorption data for the dihydronaphthyl and indenyl derivatives described above are collected in the Table. Like the parent

Ultraviolet-light absorption of dihydronaphthyl and indenyl derivatives.

			" Phenyl " band		" Styryl " band		
	R	R′	$\lambda_{max.}$ (Å)	ε	$\lambda_{max.}$ (Å)	ε	Solvent
							
(I)	H	H	—	—	2620	10,000 [a]	Hexane
(II)	Cl	H	2250	16,500	2640	8000	Hexane
(III)	H	Cl	2190	17,500	2700	6500	Hexane
			2260	13,100			
(IV)	CO_2H	H	2230	12,500	2740	6000	Ethanol
(V)	H	CO_2H	2250	20,000	2910	15,000	Ethanol
							
(VI)	H	H	—	—	2490	11,500 [a]	Ethanol
(VII)	Cl	H	2230	10,000	2510	9500	Hexane
(VIII)	H	Cl	2250	9000	2610	10,000	Hexane
(IX)	CO_2H	Cl	2280	11,000	2760	5500	Ethanol
(X)	CO_2Me	Cl	2270	16,500	2780	5500	Ethanol
					2800	6500	Dioxan

[a] Morton and de Gouveia, *J.*, 1934, 911, 916.

chromophore, styrene [$\lambda_{max.}$ 2110 (ε 16,000) and 2440 Å (ε 12,000)], they all show two bands : one near 2200 Å which may be regarded as a displaced phenyl (E_2-)band (cf. Braude, *Ann. Reports*, 1945, **42**, 105) and the other in the 2500-Å region which is associated with the substituted Ph·C=C system. The locations of the short-wavelength bands are almost independent of the substituents, but the intensities are only about half as high for the indenyl as for the dihydronaphthyl or styryl derivatives. The reason for this difference is uncertain; it is unlikely to be due to steric effects (cf. Braude and Waight in " Progress in Stereochemistry," ed. W. Klyne, Vol. I, Chapter 4, Butterworths, London, 1954), since the indenyl will, if anything, be more planar than the dihydronaphthyl system. It is therefore presumably to be ascribed either to the greater hyperconjugation in the five-membered ring or to transannular conjugation between the benzene ring and the double bond, though either effect might also be expected to lead to a wavelength displacement (cf. Braude, *Chem. and Ind.*, 1954, 1557).

The long-wavelength bands show normal bathochromic displacements which, as usual, are larger for a 2-substituent which is in a terminal position with respect to the conjugated system than for a 1-substituent (cf. Bowden, Braude, and Jones, *J.*, 1946, 948; Bowden and Braude, *J.*, 1952, 1068). Thus the values of $\Delta\lambda$ are: 1-Cl, 20 Å; 2-Cl, 120 Å; 1-CO_2H, 120 Å; and 2-CO_2H, 290 Å. On this basis, the calculated $\lambda_{max.}$ for the acid (IX) is 2730 Å (2490 + $\Delta\lambda_{1\text{-}CO_2H}$ + $\Delta\lambda_{2\text{-}Cl}$), in close agreement with that observed.

Experimental

For general methods, see Part IX, *J.*, 1955, 3324. Spectral data are only given when not included in the Table.

α-*Tetralone*.—A solution of chromium trioxide (450 g.) in water (230 ml.) and acetic acid (1200 ml.) was added, dropwise (*ca.* 500 ml./hr.) with vigorous stirring, to tetralin (240 g.) in glacial acetic acid (1300 ml.) during 3 hr.; the temperature was not allowed to rise above 12° (ice-cooling). After the mixture had been kept at 12° for a further 6 hr., it was allowed to attain room temperature and kept for 10 days. The dark green solution was diluted with water (8 l.) and extracted with ether until the extracts were almost colourless. The combined ether extracts (3 l.) were washed several times with 2N-sodium carbonate (1-l. portions) to remove acetic acid. The ether layer was dried (Na_2SO_4–K_2CO_3) and the ether removed through an 8″ Dufton column. The residue was distilled, giving unchanged tetralin (42 g.), b. p. 93—97°/10 mm., and α-tetralone (75 g., 28%), b. p. 129—135°/12 mm., n_D^{21} 1·5675. Yields up to 50% of α-tetralone can be obtained on a smaller scale [cf. Nazarov and Burmistrova, *Zhur. obshchei Khim.*, 1950, **20**, 1904].

4-*Chloro*-1 : 2-*dihydronaphthalene*.—α-Tetralone (50 g.) was added dropwise with stirring and cooling to phosphorus pentachloride (84 g.), and the mixture was stirred overnight at room temperature. Next morning, the solution was poured into ice-water (1 l.) and extracted with ether (4 × 100 ml.), and the ether extracts were washed with water (100 ml.), dried (Na_2SO_4), and fractionated through an 8″ Dufton column, giving: (i) 4-*chloro*-1 : 2-*dihydronaphthalene* (20 g., 36%), b. p. 59°/10^{-3} mm., n_D^{20} 1·5978, which after refractionation from sodium had b. p. 50—51°/10^{-4} mm., n_D^{23} 1·5952 (Found: C, 72·9; H, 5·7; Cl, 22·5. Calc. for $C_{10}H_9Cl$: C, 73·0; H, 5·5; Cl, 21·5%) (Mousseron and Jacquier, *Bull. Soc. chim. France*, 1950, 648, give b. p. 105°/2 mm., n_D^{25} 1·5810); (ii) higher-boiling fractions (16 g.), b. p. 76—82°/10^{-5} mm., n_D^{20} 1·6038—1·6092, which consisted mainly of 1 : 1-dichlorotetrahydronaphthalene and were recovered unchanged on treatment for 24 hr. with 20% alcoholic potassium hydroxide at 35°.

3 : 4-*Dihydro*-1-*naphthoic Acid*.—4-Chloro-1 : 2-dihydronaphthalene (10 g.) in anhydrous ether (25 ml.) was added dropwise to a stirred suspension of finely cut lithium (1 g.) in refluxing anhydrous ether (450 ml.). A faint turbidity appeared after 20 min. After 66 hours' refluxing, all the lithium had reacted and the solution was deep red.

This solution was poured on a large excess of finely powdered solid carbon dioxide (*ca.* 600 g.). After attaining room temperature, the mixture was diluted with water (400 ml.) and acidified dropwise with concentrated hydrochloric acid, and the ether layer was separated and extracted with 2N-sodium hydroxide (2 × 150 ml.). Evaporation of the ethereal solution under reduced pressure gave only a small amount of a dark brown gum. The aqueous alkaline extract was acidified with concentrated hydrochloric acid and extracted with ether (2 × 75 ml.), and the ethereal extracts, which exhibited a strong green fluorescence, were dried (Na_2SO_4) and evaporated under reduced pressure. The residual dark brown gum was sublimed at 10^{-5} mm., giving 3 : 4-dihydro-1-naphthoic acid (1·3 g., 12%) which crystallised from light petroleum (b. p. 60—80°) in needles, m. p. 120—122° (Found: C, 76·2; H, 6·1. Calc. for $C_{11}H_{10}O_2$: C, 75·8; H, 5·8%) (Fieser and Holmes, *J. Amer. Chem. Soc.*, 1936, **58**, 2319, 2321, give m. p. 121°). Infrared absorption (paraffin mull): $\nu_{max.}$ 2650, 2580 (OH stretching), 1670 (C=O stretching), 1608 (C=C stretching), and 917 $cm.^{-1}$ (OH deformation). The *benzylamine salt* crystallised from ethyl acetate–ethanol in needles, m. p. 145—146° (Found: C, 76·1; H, 6·35; N, 4·9. $C_{18}H_{19}O_2N$ requires C, 76·8; H, 6·8; N, 5·0%).

When the acid (0·2 g.) was heated with 10% palladium–charcoal (0·05 g.) at 290—300° for 5—6 hr. in a stream of nitrogen, naphthalene (0·1 g., 68%), m. p. and mixed m. p. 80°, was obtained.

Attempted Formylation of 3 : 4-*Dihydro*-1-*naphthyl-lithium*.—Dimethylformamide (3·8 g.) in anhydrous ether (25 ml.) was added dropwise to 3 : 4-dihydro-1-naphthyl-lithium (from metal, 0·8 g., and 4-chloro-1 : 2-dihydronaphthalene, 7·5 g.), in ether (300 ml.) at 0°. The mixture was stirred at room temperature for 2 hr. and then treated with a saturated solution of ammonium

chloride (300 ml.). The ether layer was separated, dried (Na_2SO_4), and fractionated, giving a mixture (2·4 g.), b. p. 135—145° (bath-temp.)/10^{-4} mm., n_D^{19} 1·6352, which did not give a semicarbazone but yielded a 2 : 4-*dinitrophenylhydrazone*, which after chromatography on alumina in benzene–chloroform crystallised from ethyl acetate–methanol in orange plates, m. p. 203—204°, $\lambda_{max.}$ 3860 Å (ε 27,000 in $CHCl_3$) (Found : C, 58·3; H, 4·6; N, 15·3. $C_{17}H_{14}O_4N_4.H_2O$ requires C, 57·3; H, 4·5; N, 15·7%). The analytical data correspond to a hydrate of the derivative of 3 : 4-dihydro-1-naphthaldehyde.

4-*Chloro*-1 : 2-*dihydronaphthalene*.—β-Tetralone (56 g., prepared by the method of Birch, *J.*, 1944, 430) was added dropwise with stirring and cooling to phosphorus pentachloride (100 g.) during 15 min. The mixture was stirred for 3 hr. at room temperature and then poured into ice-water (1 l.). Working up as above gave 3-*chloro*-1 : 2-*dihydronaphthalene* (21 g., 34%), b. p. 60°/0·1 mm., n_D^{21} 1·5870 (Found : C, 73·3; H, 5·55. $C_{10}H_9Cl$ requires C, 73·0; H, 5·5%).

3 : 4-*Dihydro*-2-*naphthoic Acid*.—3-Chloro-1 : 2-dihydronaphthalene (10 g.; redistilled from sodium) was added to a stirred suspension of finely cut lithium (1 g.) in refluxing anhydrous ether (400 ml.). The solution became slightly turbid after 15 min., then gradually acquired a violet colour which was intense after 1 hr. and gradually changed to orange after 6 hr. After 24 hours' refluxing, all the metal had been consumed and the solution was deep red.

Carboxylation of this solution as above gave 3 : 4-dihydro-2-naphthoic acid (0·9 g., 8%) which was isolated from the accompanying polymeric material by sublimation at 10^{-4} mm. and crystallised from light petroleum (b. p. 60—80°) in plates, m. p. 118° (Found : C, 76·0; H, 5·6. Calc. for $C_{11}H_{10}O_2$: C, 75·9; H, 5·75%) (Derick and Kamm, *J. Amer. Chem. Soc.*, 1916, **38**, 400, 409, give m. p. 118·5°). Infrared absorption (paraffin mull) : $\nu_{max.}$ 2710, 2660 (OH stretching), 1675 (C=O stretching), and 1623 $cm.^{-1}$ (C=C stretching). The *benzylamine salt* crystallised in colourless needles (from ethyl acetate), m. p. 154—155° (Found : C, 76·8; H, 6·6; N, 3·2. $2C_{11}H_{10}O_2.C_7H_9N$ requires C, 76·5; H, 6·4; N, 3·1%).

2-*Chloroindene*.—Dry chlorine was passed into a well-cooled solution of indene (156 g.) in carbon tetrachloride (400 ml.). The theoretical amount of chlorine (95 g.) was taken up during 1·5 hr. The solvent was distilled off through an 8″ Dufton column and the residue fractionated under reduced pressure, giving 1 : 2-dichloroindane (185 g.), b. p. 86—90°/2 mm., n_D^{23} 1·5715 (Suter and Lutz, *J. Amer. Chem. Soc.*, 1938, **60**, 1360, give b. p. 98—102°/5 mm., n_D^{25} 1·5710).

1 : 2-Dichloroindane (75 g.) was heated for 5 hr. at 225—235° until the vigorous evolution of hydrogen chloride subsided. Fractionation of the residue gave 2-chloroindene (35 g.), b. p. 110—116°/13 mm., n_D^{23} 1·5797—1·5817, which on refractionation from sodium had b. p. 100—104°/11 mm., n_D^{23} 1·5823 (Suter and Lutz, *loc. cit.*, give b. p. 95—98°/11 mm., n_D^{25} 1·5824). Infrared absorption (liquid film) : strong peaks at 1642, 1592, 1563, and 749 $cm.^{-1}$.

2-*Chloroindenyl*-3-*carboxylic Acid*.—2-Chloroindene (12 g.), freshly distilled from sodium, was added to a stirred suspension of lithium (1·4 g.) in refluxing anhydrous ether (450 ml.). After 10 min. the mixture became slightly turbid, after approximately 12 hours' refluxing it had a violet colour, but most of the lithium had not reacted, and after a total reflux time of 112 hr. it was greyish-green. Filtration through glass wool gave unchanged lithium (0·6 g.) which was pyrophoric. The solution was added to a large excess of powdered carbon dioxide (*ca.* 600 g.) and then allowed to attain room temperature. Water (300 ml.) was added, the solution was acidified with concentrated hydrochloric acid, and the ether layer was separated and extracted with 2N-sodium carbonate (2 × 250 ml.). Acidification of the sodium carbonate solution with concentrated hydrochloric acid gave a yellow solid (2·8 g.), and a further quantity (0·3 g.) was obtained by extraction with ether. Recrystallisation of the solid product from benzene gave 2-*chloroindenyl*-3-*carboxylic acid* as very pale yellow needles, m. p. 184—185° [Found : C, 61·6; H, 3·85; Cl, 18·1%; *M* (in camphor), 197; equiv., 193. $C_{10}H_7O_2Cl$ requires C, 61·7; H, 3·6; Cl, 18·2%; *M* and equiv., 195). Infrared absorption (paraffin mull) : main peaks at 2618 (OH stretching), 1692 (CO_2H), and 1587 $cm.^{-1}$ (C=C stretching). Treatment of the acid in ether with ethereal diazomethane gave the *methyl ester*, which crystallised from pentane at −60° in pale yellow needles, m. p. 47° (Found : C, 63·2; H, 4·5; Cl, 17·2. $C_{11}H_9O_2Cl$ requires C, 63·3; H, 4·3; Cl, 17·0%).

3-*Chloroindene*.—Indan-1-one (60 g.) in dry benzene (30 ml.) was added dropwise with cooling to phosphorus pentachloride (100 g.), in dry benzene (50 ml.), during 1 hr. The mixture was stirred for a further 3 hr. and then poured on crushed ice (*ca.* 500 g.). Isolation of the product with ether and fractionation gave 1-chloroindene (35 g.), b. p. 109—110°/16 mm., n_D^{23} 1·5808 (Found : C, 72·1; H, 5·2; Cl, 22·8. Calc. for C_9H_7Cl : C, 71·8; H, 4·7; Cl, 23·7%) (Braun and Ostermayer, *Ber.*, 1937, **70**, 1006, give b. p. 105°/15 mm.). Infrared absorption (paraffin mull) : main peaks at 1613, 1590, 1560, and 757 $cm.^{-1}$.

Attempts to metallate 3-chloroindene with lithium in refluxing ether were unsuccessful; most of the metal was recovered unchanged even after 60 hours' refluxing, and only a slight turbidity and a pale green colour were observed.

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Experiments on the Synthesis of Substances Related to the Sterols. Part LII. Some Condensations of Substituted β-Diketones including an Account of a New Molecular Rearrangement.*

By A. R. PINDER and SIR ROBERT ROBINSON.

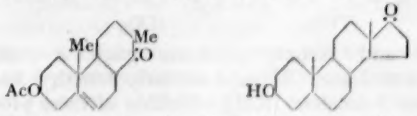
[Reprint Order No. 6269.]

Model experiments designed to test a possible method of adding ring D to an ABC-tricyclic system, such as is found in a steroid degradation product, are described. Two stages of acetylation of ketones R·CHMe·COR′ with acetic anhydride and boron trifluoride afforded R′·CO·CMeR·CO·CH_2·COMe in poor yield. Efforts to cyclise these triketones were unsuccessful.

Condensation of 2-methyl-*trans*-1-decalone with 1 : 3-dichlorobut-2-ene, followed by cyclisation, gave a BCD-tricyclic ketone. Reduction of the double bond by various methods invariably resulted in a *cis*-C/D-junction.

α-Acetyl*iso*butyrophenone was converted by sodium in ethereal medium into ω-*iso*butyrylacetophenone (1 : 3-dioxo*iso*hexylbenzene). This molecular rearrangement has not been previously observed among straight-chain compounds. It is analogous to certain transformations of cyclic keto-esters and to the Baker–Venkataraman change.

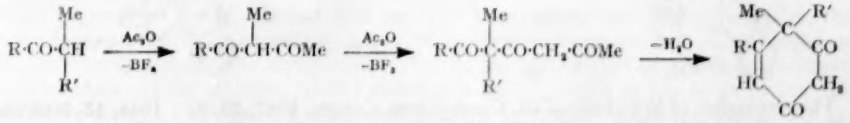
THE isolation of the ABC-tricyclic keto-acetate (I) as a steroid oxidative degradation product by Köster and Logemann (*Ber.*, 1940, **73**, 298) stimulated investigations of the possibility of adding ring D to such a system, so as to regenerate the steroid framework as in androsterone



(I) (II)

(II). The present communication describes investigations, with model ketones, of a new possible method of fusion of a ring D to an ABC-tricyclic system, but the outcome was not encouraging.

Meerwein and his co-workers (*Ber.*, 1933, **66**, 411; *J. prakt. Chem.*, 1934, **141**, 149) and Adams and Hauser (*J. Amer. Chem. Soc.*, 1944, **66**, 345; 1945, **67**, 284) have shown that ketones containing reactive $\geqslant$CH, $>CH_2$, or $-CH_3$ groups can be acylated with acid anhydrides and boron trifluoride with formation of the corresponding α-acyl-ketones. We contemplated the use of this reaction to provide a six-membered ring (which might be degraded to a five-membered ring) as shown in the following scheme, using acetic anhydride as acylating agent :

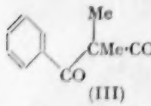


Several α-methyl-ketones have been used as models in these reactions. We have confirmed that, in the presence of boron trifluoride, the corresponding α-acetyl-α-methyl-ketone can be obtained in moderate yield.

*iso*Butyrophenone afforded α-acetyl*iso*butyrophenone (III); and further acetylation of this diketone gave 5-benzoyl-5-methylhexane-2 : 4-dione (IV), but in very poor yield.

* Part LI, *J.*, 1953, 361. The results reported in the present paper formed part of a Thesis (A. R. P.) submitted in May, 1950.

A small quantity of the latter substance was isolated from the reaction mixture in the first stage of acetylation; in fact, in every case we have examined, a small quantity of the triketone accompanied the monoacetylated ketone.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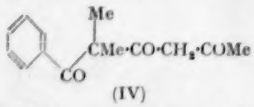
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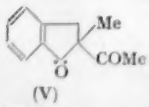
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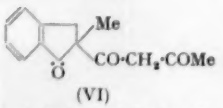
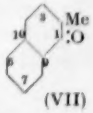

(VI)

The acetylation in this manner of 2-methylindan-1-one afforded 2-acetyl-2-methylindan-1-one (V) and 2-acetoacetyl-2-methylindan-1-one (VI), the latter in very poor yield. Similarly, 2-methyl-*trans*-1-decalone (VII) gave 2-acetyl-2-methyl-*trans*-1-decalone (VIII), and further acetylation gave 2-acetoacetyl-2-methyl-*trans*-1-decalone (IX). There is, in the case of 2-methyl-*trans*-1-decalone, some doubt about the position taken up by the first acetyl group, as the ketone has an angular $\geqslant$CH group adjacent to the carbonyl group. From steric considerations, we are of the opinion that the acetyl group has entered the 2-position, but the possibility that the product contains some 9-acetyl-2-methyl-*trans*-1-decalone (X) cannot be ruled out since Adams and Hauser (*loc. cit.*) have shown that acetylation of systems of the type $>$CH·CO·CH$<$ may give isomeric products.

Attempts to effect the cyclisation of the acetoacetyl-ketones were unsuccessful. With aqueous acids or bases, hydrolysis occurred very readily, whilst with anhydrous catalysts complex condensations took place or the compounds were unaffected. The failure to cyclise may perhaps be accounted for by the fact that these ketones are highly enolised. They were all readily soluble in aqueous alkali, gave intense red colours with ferric chloride, and formed copper complexes.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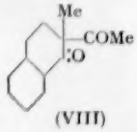
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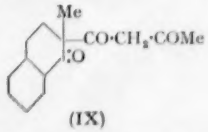
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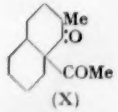
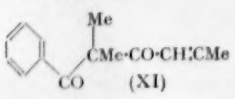
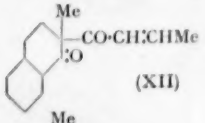

(X)

Crotonic anhydride and *iso*butyrophenone gave α-crotonoyl*iso*butyrophenone (2-benzoyl-2-methylhex-4-en-3-one) (XI), and similarly 2-methyl-*trans*-1-decalone furnished 2-crotonoyl-2-methyl-*trans*-1-decalone (XII). Neither of these products could be cyclised to a six-membered ring-ketone. Oxidation of the ketone (XII) with permanganate gave 2-methyl-1-decalone-2-carboxylic acid (XIII), identical with the acid obtained by Dr. H. Holtermann, in this laboratory, by the carboxylation of 2-methyl-*trans*-1-decalone with sodium triphenylmethyl and carbon dioxide. The position of the crotonoyl side-chain is therefore established.


(XI)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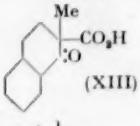
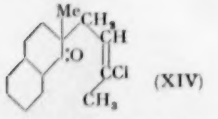

(XIII)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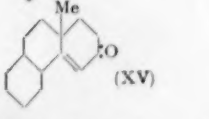
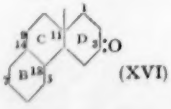
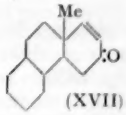

(XV)


(XVI)

The researches of Wichterle (*Coll. Czech. Chem. Comm.*, 1947, **12**, 93; 1948, **13**, 300) and of Prelog, Barman, and Zimmermann (*Helv. Chim. Acta*, 1949, **32**, 1284) have shown that 1 : 3-dichlorobut-2-ene condenses with enolisable ketones and esters, and the products can be cyclised smoothly. We have found that 2-methyl-*trans*-1-decalone condenses with 1 : 3-dichlorobut-2-ene to give 2-(3-chlorobut-2-enyl)-2-methyl-*trans*-1-decalone (XIV), which cyclised with sulphuric acid to $\Delta^{4(14)}$-dodecahydro-11-methyl-3-oxophenanthrene (XV) (cf. Pinder and Robinson, *J.*, 1952, 1224, for an analogous preparation starting from 1-methyl-*cis*-α-decalone), identical with the product obtained in this laboratory by Dr. H.

Holtermann by condensation of 2-methyl-*trans*-1-decalone with 4-diethylaminobutan-2-one methiodide. Catalytic hydrogenation gave perhydro-11-methyl-3-oxophenanthrene (XVI). The C/D-junction in this compound was almost certainly *cis*, because bromination and dehydrobromination of the saturated ketone (XVI) regenerated the unsaturated ketone (XV), and not the isomeric product (XVII), the intermediate bromo-ketone being 4-bromo-perhydro-11-methyl-3-oxophenanthrene (XVIII) (cf. Butenandt and Wolff, *Ber.*, 1935, **68**, 2091).



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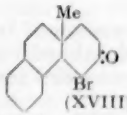

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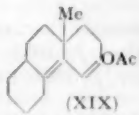

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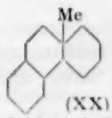
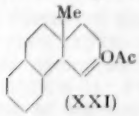
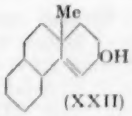


(XX)

Treatment of the enone (XV) with acetyl chloride and acetic anhydride (cf. Inhoffen, *Ber.*, 1936, **69**, 2146) afforded an enol acetate, which because of its ultraviolet absorption spectrum appeared to be 3-acetoxy-$\Delta^{3:12}$-decahydro-11-methylphenanthraene (XIX). Catalytic hydrogenation of the enol acetate using Adams platinum oxide gave perhydro-11-methylphenanthrene (XX), whilst use of palladised strontium carbonate afforded an intermediate enol acetate (XXI) (not isolated), which was converted by hydrolysis into the saturated ketone (XVI), so that the 12 : 13-double bond was reduced in preference to that at the 3 : 4-position.



(XXI)



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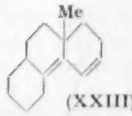

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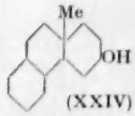


(XXIV)

Reduction of the enone (XV) by Ponndorf's method (cf. Schoenheimer and Evans, *J. Biol. Chem.*, 1936, **114**, 567) gave a mixture of epimerides of $\Delta^{4(12)}$-dodecahydro-3-hydroxy-11-methylphenanthrene (XXII). Dehydration of this alcohol with acid gave $\Delta^{3:12}$-decahydro-11-methylphenanthrene (XXIII), the position of the double bonds being established by the ultraviolet absorption spectrum.

Reduction of the unsaturated ketone (XV) with sodium and *iso*pentyl alcohol gave perhydro-3-hydroxy-11-methylphenanthrene (XXIV) as a mixture of stereoisomerides. Oxidation of this alcohol by means of chromic acid afforded the saturated ketone (XVI), with a *cis*-C/D-configuration.

When an attempt was made to condense the diketone (III) and ethyl acetate with the help of sodium, the triketone (IV) was not produced but, instead, *ω-iso*butyrylacetophenone (4-methyl-1-phenylpentane-1 : 3-dione) (XXV) (Stylo, Beyer, and Claisen, *Ber.*, 1887, **20**, 2181). The same result was obtained without the use of ethyl acetate. The rearrangement of the diketone (III) might be intramolecular or intermolecular, but a third possibility, that of fission and resynthesis, is perhaps the most natural explanation.

If we postulate intramolecular rearrangement, or intermolecular double decomposition, there can be no theoretical difficulty in bringing the new case into line with the usual β-diketone synthesis.

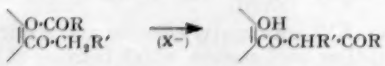
All β-diketones contain bound acyl residues from which the related acids or their derivatives can readily be generated, for example, by hydrolysis, alcoholysis, or aminolysis. The carbonyl groups of these acyl groups are markedly cationoid in electrochemical character and can therefore be attacked by the electron-donating anions of the enols of the keto-methylene groups. Fission will supervene and the net result is the transfer of the acyl group from a certain position to another similar but more stable union.

$CHMe_2{\cdot}CO{\cdot}CH_2{\cdot}COPh$ (XXV) $\qquad R{\cdot}CO{\cdot}CR'R''{\cdot}CO{\cdot}CH_3 \longrightarrow CHR'R''{\cdot}CO{\cdot}CH_2{\cdot}COR$

The closest formal analogy of which we are aware is provided by the annexed transformation of certain esters in the *cyclo*hexanone series (Openshaw and Robinson, *J.*, 1937, 941). This process, however, almost certainly proceeds by ring-opening alcoholysis and Dieckmann-type ring-closure of the resulting substituted pimelic ester. Fission and

recombination is an obvious possibility in the new case but would require the presence of a catalytic quantity of alcohol (sodium ethoxide). Actually a trace of alcohol was added to the ethereal solution, so that this condition was satisfied.

Another analogous process is the internal acylation of ketones established by Baker and by Venkataraman (Baker, *J.*, 1933, 1381; Mahal and Venkataraman, *J.*, 1934, 1767; Nowlan, Slavin, and Wheeler, *J.*, 1950, 340; Gowan and Wheeler, *ibid.*, p. 1925):



Until it is established that the new reaction is intramolecular, or intermolecular, or involves the intervention of another substance such as alcohol leading to fission and recombination, it is unnecessary to speculate about the detailed mechanism. In any case there can be no difficulty in representation of the reaction as essentially a β-diketone synthesis of Claisen type.

Experimental

iso*Butyrophenone*.—The Friedel–Crafts reaction between benzene and *iso*butyryl chloride (Schmidt, *Ber.*, **1889**, **22**, 3250) gave phenyl *iso*propyl ketone, b. p. 93—97°/11 mm., in 48% yield. The 2 : 4-*dinitrophenylhydrazone* separated from ethyl acetate as orange, elongated prisms, m. p. 159° (Found: C, 58·1; H, 4·8. $C_{16}H_{16}O_4N_4$ requires C, 58·5; H, 4·9%).

α-*Acetylisobutyrophenone* (3-*Benzoyl*-3-*methylbutan*-2-*one*) (III).—A mixture of *iso*butyrophenone (20 g.) and acetic anhydride (27·5 g.) was saturated with boron trifluoride at 0° during 1·5 hr., the increase in weight being 19·5 g. The dark syrup was poured into a cold solution of crystallised sodium acetate (45 g.) in water (100 c.c.), and the oil extracted with ether. The ethereal solution was extracted several times with 5% sodium hydroxide solution, dried, and distilled. The residue was distilled *in vacuo* through a 20-cm. lagged Dufton column, giving α-acetyl*iso*butyrophenone, b. p. 125—128°/14 mm. (14 g.) (Found: C, 75·6; H, 7·5. Calc. for $C_{12}H_{14}O_2$: C, 75·8; H, 7·4%). Morton, Hassan, and Calloway (*J.*, 1934, 891) give b. p. 84°/2 mm. The diketone was a pale yellow liquid, insoluble in dilute alkali. It gave no colour with ferric chloride, and formed no copper complex. Hydrolysis by boiling with dilute alkali gave *iso*butyrophenone, methyl *iso*propyl ketone, and acetic and benzoic acid.

The *monoxime* separated from aqueous ethanol in clusters of elongated prisms, m. p. 148° (Found: C, 70·2; H, 7·2. $C_{12}H_{15}O_2N$ requires C, 70·2; H, 7·3%). The *monosemicarbazone* crystallised from ethanol in elongated prisms, m. p. 167—168° (Found: C, 63·2; H, 7·0. $C_{13}H_{17}O_2N_3$ requires C, 63·2; H, 6·9%). The *bis*-2 : 4-*dinitrophenylhydrazone* was dimorphous, one form separating from ethyl acetate in small red prisms, m. p. 136° (Found: C, 52·4; H, 4·1%), and the other in red prisms, m. p. 197—198° (Found: C, 52·2; H, 4·4. $C_{24}H_{22}O_8N_8$ requires C, 52·4; H, 4·0%).

Acidification of the alkaline washings gave an oil which was taken up in ether and washed with sodium hydrogen carbonate. Evaporation of the ethereal solution left an oil (1·0 g.), identified as 5-benzoyl-5-methylhexane-2 : 4-dione (see below).

Reaction of α-Acetylisobutyrophenone with Sodium.—A solution of the diketone (7·6 g.) in ether (5 c.c.), containing one drop of alcohol, was added to a suspension of sodium wire (2·0 g.) in dry ether (20 c.c.). The mixture was kept for 24 hr. after which the unchanged sodium was destroyed by addition of a little alcohol, and ice was added. The aqueous layer was extracted twice with ether, then acidified, and the product isolated with ether. After drying and evaporation a yellow oil remained, which distilled at 125—130°(bath)/0·15 mm. (1·5 g.). This diketone was converted into its copper complex, which separated from light petroleum (b. p. 60—80°) in dark green prisms, m. p. 161—162°. Decomposition of the complex with dilute sulphuric acid and ether gave an oil which distilled at 115—120°(bath)/0·2 mm. (1·3 g.) (Found: C, 75·4; H, 7·2. Calc. for $C_{12}H_{14}O_2$: C, 75·8; H, 7·4%).

With 2 : 4-*dinitrophenylhydrazine* the product gave 1-(2 : 4-*dinitrophenyl*)-3-*phenyl*-5-*isopropylpyrazole*, which separated from alcohol as golden-yellow rhombs, m. p. 144° (Found: C, 61·2; H, 4·6; N, 15·9. $C_{18}H_{16}O_4N_4$ requires C, 61·3; H, 4·5; N, 15·9%).

Alkaline hydrolysis of the original product gave benzoic acid, acetophenone, and *iso*butyric acid (anilide, m. p. 105°).

*iso*Butyrylacetophenone (4-methyl-1-phenylpentane-1 : 3-dione), prepared as described by Stylos, Beyer, and Claisen (*Ber.*, 1887, **20**, 2181) from acetophenone and ethyl *iso*butyrate, distilled at 125—130°(bath)/0·2 mm. and gave a copper complex and a pyrazole identical (m. p., mixed m. p., etc.) with the derivatives described above.

5-Benzoyl-5-methylhexane-2 : 4-dione (IV).—A solution of α-acetyl*iso*butyrophenone (9·5 g.) in acetic anhydride (10·2 g.) was saturated with boron trifluoride at 0° during 1 hr. The syrupy product was poured into a solution of sodium acetate (25 g.) in water (50 c.c.), and the oil which separated taken up in ether. The ethereal solution was repeatedly extracted with cold dilute alkali until an extract, after acidification, gave no ferric reaction. The combined alkaline extracts were acidified and the oil was extracted with ether. The ethereal solution was washed with sodium hydrogen carbonate, dried, and distilled. *5-Benzoyl-5-methylhexane-2 : 4-dione* was obtained as a pale yellow oil, b. p. 140—143°(bath)/1 mm. (1·5 g.) (Found : C, 72·5; H, 6·9. $C_{14}H_{16}O_3$ requires C, 72·4; H, 6·9%). The substance developed a wine-red colour with ferric chloride, and was readily soluble in dilute alkali. Alkaline hydrolysis gave benzoic acid, *iso*butyrophenone, acetone, and methyl *iso*propyl ketone. The copper complex, prepared by shaking an ethereal solution of the triketone with a saturated solution of cupric acetate, separated from a large volume of light petroleum (b. p. 60—80°) in pale blue prisms, m. p. 192°. The *monosemicarbazone* crystallised from ethanol in elongated prisms, m. p. 169—170° (decomp.) (Found : C, 61·9; H, 6·7; N, 14·4. $C_{15}H_{19}O_3N_3$ requires C, 62·3; H, 6·6; N, 14·5%). Attempts to cyclise the triketone were unsuccessful.

*α-Crotonoyliso**butyrophenone** (2-Benzoyl-2-methylhex-4-en-3-one)* (XI).—A solution of *iso*butyrophenone (5 g.) in crotonic anhydride (10·6 g.; Glover and Richmond, *Amer. Chem. J.*, 1903, **29**, 194) was saturated with boron trifluoride at 0° during 1 hr. The dark syrup was decomposed with a solution of sodium acetate (20 g.) in water (50 c.c.). The product, isolated by means of ether, was fractionated *in vacuo* : *α-crotonoyliso**butyrophenone*** (4·0 g.) distilled at 125—127°(bath)/0·75 mm. (Found : C, 77·8; H, 7·5. $C_{14}H_{16}O_2$ requires C, 77·8; H, 7·4%). Alkaline hydrolysis afforded *iso*butyrophenone, and benzoic and crotonic acids. The *disemicarbazone* separated from ethanol in elongated prisms, m. p. 265° (decomp.) (Found : C, 58·3; H, 6·5; N, 26·0. $C_{16}H_{22}O_2N_6$ requires C, 58·2; H, 6·7; N, 25·5%). Cyclisation of the diketone could not be effected.

2-Acetyl-2-methyl-indan-1-one (V).—A mixture of 2-methylindan-1-one (Kipping and Clarke, *J.*, 1903, **83**, 915) (7·3 g.) and acetic anhydride (10·2 g.) was saturated with boron trifluoride at 0°. The mixture, worked up in the usual manner, gave on distillation *2-acetyl-2-methylindan-1-one* (4·7 g.), b. p. 135—140°(bath)/0·7 mm. (Found : C, 76·5; H, 6·2. $C_{12}H_{12}O_2$ requires C, 76·6; H, 6·4%). Alkaline hydrolysis gave methylindanone and acetic acid. The *bis-2 : 4-dinitrophenylhydrazone* separated from ethyl acetate as orange-red rhombs, m. p. 143° (decomp.) (Found : C, 53·0; H, 4·3. $C_{24}H_{20}O_8N_8,C_4H_8O_2$ requires C, 52·8; H, 4·4%). The *monosemicarbazone* separated from ethanol in elongated prisms, m.p. 211° (Found : C, 63·3; H, 6·4. $C_{13}H_{15}O_2N_3$ requires C, 63·7; H, 6·1%).

A small quantity of 2-acetoacetyl-2-methylindan-1-one (see below) was also obtained in this reaction.

2-Acetoacetyl-2-methylindan-1-one (VI).—A solution of 2-acetyl-2-methylindan-1-one (18·8 g.) in acetic anhydride (20·4 g.) was saturated with boron trifluoride at 0°. Decomposition of the mixture in the usual manner, followed by extraction with alkali, afforded *2-acetoacetyl-2-methylindan-1-one* (3·0 g.) which distilled at 150°(bath)/0·1 mm. (Found : C, 73·3; H, 6·2. $C_{14}H_{14}O_3$ requires C, 73·0; H, 6·1%). The triketone was readily soluble in dilute alkali and gave a wine-red ferric colour. The copper complex separated from benzene in dark green prisms, m. p. 147—148°. With 6 : 6′-diaminoveratrone, a *copyrine* was obtained (cf. Lawson, Perkin, and Robinson, *J.*, 1924, **125**, 630, 647), which separated from nitrobenzene in dull yellow needles, m. p. >280° (Found : N, 5·4. $C_{31}H_{28}O_5N_2$ requires N, 5·5%).

Attempts to effect an intramolecular cyclisation of the triketone were unsuccessful.

2-Methyl-trans-1-decalone (VII).—The synthesis of this ketone was effected from 1-naphthol by the procedure described by Dr. E. B. J. Smith (D.Phil. Thesis, Oxford, 1949). The *2 : 4-dinitrophenylhydrazone* separated from ethyl acetate in red needles, m. p. 239° (decomp.) (Found : C, 58·8; H, 6·0; N, 15·8. $C_{17}H_{22}O_4N_4$ requires C, 58·9; H, 6·3; N, 16·2%).

The *semicarbazone* crystallised from 60% ethanol in stout prisms, m. p. 221° (Found : C, 64·6; H, 9·4. $C_{12}H_{21}ON_3$ requires C, 64·6; H, 9·4%). The discrepancies in m. p. between these derivatives and those of the 2-methyl-1-decalone described by Cook and Lawrence (*J.*,

1937, 818) are to be ascribed to stereochemical differences; it is probable that the product obtained by these authors was not stereochemically homogeneous.

2-Acetyl-2-methyl-trans-*1-decalone* (VIII).—A mixture of 2-methyl-*trans*-1-decalone (8·3 g.) and acetic anhydride (10·2 g.) was saturated with boron trifluoride at 0°. The mixture was worked up in the usual manner. Fractional distillation gave 2-acetyl-2-methyl-1-decalone (7·5 g.), b. p. 122—125°(bath)/0·25 mm. (Found: C, 75·7, 75·6; H, 10·0, 13·2. Calc. for $C_{13}H_{20}O_2$: C, 75·0; H, 9·6%). Owing to the difficulty of separating the product completely from unchanged 2-methyl-1-decalone, better analytical figures could not be obtained. Alkaline hydrolysis gave 2-methyl-1-decalone and acetic acid. The *monosemicarbazone* separated from methyl alcohol in minute prisms, m. p. 239—240° (decomp.) (Found: C, 63·5; H, 8·4; N, 15·9. $C_{14}H_{23}O_2N_3$ requires C, 63·4; H, 8·7; N, 15·8%).

2-Acetoacetyl-2-methyl-1-decalone (IX).—Saturation of a mixture of 2-acetyl-2-methyl-1-decalone (7·0 g.) and acetic anhydride (7·0 g.) with boron trifluoride at 0° gave a small yield (0·5 g.) of the alkali-soluble *2-acetoacetyl-2-methyl-1-decalone*, b. p. 160°(bath)/0·2 mm. (Found: C, 71·6; H, 8·8. $C_{15}H_{22}O_3$ requires C, 72·0; H, 8·8%). The triketone gave an intense wine-red ferric reaction, and formed a greenish-blue copper complex, which did not crystallise. Attempts to cyclise the triketone were unsuccessful.

2-Crotonoyl-2-methyl-1-decalone (XII).—A mixture of 2-methyl-*trans*-1-decalone (10 g.) and crotonic anhydride (18·6 g.) was saturated with boron trifluoride at 0°, and the mixture decomposed in the usual manner. Isolation of the product with ether and distillation gave *2-crotonoyl-2-methyl-1-decalone* (6·2 g.), b. p. 108—110°/0·1 mm. (Found: C, 76·4; H, 9·4. $C_{15}H_{22}O_2$ requires C, 76·9; H, 9·4%). Alkaline hydrolysis afforded 2-methyl-*trans*-1-decalone and crotonic acid. Attempts to cyclise the diketone failed. Oxidation with potassium permanganate gave 2-methyl-1-decalone-2-carboxylic acid (XIII), m. p. 117°, alone or when mixed with a specimen obtained by Dr. H. Holtermann by carboxylation of 2-methyl-1-decalone.

1 : 3-Dichlorobut-2-ene.—The commercial product was washed with sodium hydrogen carbonate, dried ($CaCl_2$), and distilled, giving the pure *trans*-form, b. p. 127—128° (Hatch and Ballin, *J. Amer. Chem. Soc.*, 1949, **71**, 1039).

$\Delta^{4(12)}$-Dodecahydro-11-methyl-3-oxophenanthrene (XV).—2-Methyl-*trans*-1-decalone (5·5 g.) in dry ether (25 c.c.) was added to an ethereal solution of sodium triphenylmethyl (300 c.c. of 0·11M; "Organic Reactions," Vol. I, p. 286), with swirling and cooling under dry nitrogen. After 30 min., 1 : 3-dichlorobut-2-ene (4·2 g.) in ether (25 c.c.) was added, with shaking. After being kept at room temperature overnight, the mixture was refluxed for 4 hr. Water was added to the cooled mixture, and the ethereal layer dried and evaporated. The syrupy residue was triturated with a little methanol and kept at 0° for several hours. The deposit of triphenylmethane was collected and washed with a little cold methanol. Evaporation of the filtrate gave an oil which was fractionated *in vacuo*. 2-(3-Chlorobut-2-enyl)-2-methyl-1-decalone (XIV) distilled at 100—110°/0·08 mm. (4·9 g.). Some unchanged 2-methyl-*trans*-1-decalone was obtained as a fore-run, and triphenylmethane appeared in higher fractions. The product was not further purified.

This chloro-ketone (2·0 g.) and concentrated sulphuric acid (2 c.c.) were carefully mixed with cooling, and kept at the room temperature overnight. Ice was added and the oil which separated taken up in ether. The ethereal solution was washed with sodium hydrogen carbonate solution and water and dried. Evaporation gave a yellow oil (1·3 g.) which was dissolved in light petroleum (b. p. 40—60°) and purified by absorption on an alumina column. Elution with benzene furnished *Δ^4-dodecahydro-11-methyl-3-oxophenanthrene*, b. p. 140—145°(bath)/ 0·05 mm. (1·1 g.) (Found: C, 82·4; H, 10·3. $C_{15}H_{22}O$ requires C, 82·6; H, 10·1%). The ketone was a pale yellow oil, having a strong ultraviolet absorption band at 245 mμ (log ε 3·9). The *semicarbazone* crystallised from methanol in colourless rhombs, m. p. 230·5° (decomp.) (Found: C, 69·7; H, 8·8. $C_{16}H_{25}ON_3$ requires C, 69·8; H, 9·1%); this derivative was sensitive to light, gradually becoming greenish-yellow. It proved to be identical with the semicarbazone obtained by Dr. H. Holtermann (*loc. cit.*) from 2-methyl-*trans*-1-decalone and 4-diethylaminobutan-2-one methiodide. The *2 : 4-dinitrophenylhydrazone* separated from ethyl acetate in deep red plates, m. p. 208° (Found: C, 62·8; H, 6·4. $C_{21}H_{26}O_4N_4$ requires C, 63·3; H, 6·5%).

Perhydro-11-methyl-3-oxophenanthrene (XVI).—A solution of the above unsaturated ketone (0·37 g.) in ethanol (8 c.c.) was shaken with a little Adams platinic oxide in an atmosphere of hydrogen at room temperature and pressure. The theoretical absorption for the reduction of one double bond was complete in 1 hr. The *perhydro-ketone* produced distilled at 135—138° (bath)/0·07 mm. (0·35 g.) (Found: C, 81·7; H, 10·7. $C_{15}H_{24}O$ requires C, 81·8; H, 10·9%).

The *semicarbazone* separated from a large volume of methanol in plates, m. p. 231—232° (Found : C, 69·2; H, 9·9. $C_{16}H_{27}ON_3$ requires C, 69·3; H, 9·7%) ; it was not light-sensitive.

4-Bromoperhydro-11-methyl-3-oxophenanthrene (XVIII).—Perhydro-11-methyl-3-oxophenanthrene (0·5 g.) in carbon tetrachloride (5 c.c.) was heated under reflux on the steam-bath with *N*-bromophthalimide (0·55 g.) for 30 min. The cooled solution was freed from phthalimide by filtration. Evaporation of the filtrate afforded 4-bromoperhydro-11-methyl-3-oxophenanthrene (0·8 g.) as a syrup, which was not purified ; free hydrogen bromide was in evidence.

Dehydrobromination by heating the whole crude product in lutidine (20 c.c.) at 170° under reflux gave an unsaturated ketone identical with Δ^1-dodecahydro-11-methyl-3-oxophenanthrene (XVII) (semicarbazone, m. p. 230—230·5°, and 2 : 4-dinitrophenylhydrazone, m. p. 208°, alone or mixed with authentic specimens).

3-Acetoxy-$\Delta^{3:12}$-decahydro-11-methylphenanthrene (XIX).—Δ^1-Dodecahydro-11-methyl-3-oxophenanthrene (0·3 g.), acetic anhydride (3 c.c.), and acetyl chloride (4·5 c.c.) were refluxed for 4 hr., the acetyl chloride being slowly distilled. The mixture was finally refluxed for a further hour, and the solvents were evaporated *in vacuo*. The residual oil was taken up in ether, and the solution washed with sodium hydrogen carbonate and with water, dried, and evaporated. The *enol acetate* distilled at 145—150°(bath)/0·03 mm. (0·3 g.) (Found : Ac, 16·7. $C_{17}H_{24}O_2$ requires Ac, 16·5%). The acetate showed maximum absorption in the ultraviolet region at 240 mμ (log ε 3·7). It gave a yellowish-brown colour with tetranitromethane in chloroform. Acid or alkaline hydrolysis regenerated the original unsaturated ketone.

Perhydro-11-methylphenanthrene (XX).—The above enol acetate (0·5 g.) in ethanol (8 c.c.) was shaken with Adams platinum oxide in an atmosphere of hydrogen at the room temperature and pressure. After 2 hr., reduction was complete, 3 mols. being absorbed. The solution, now strongly acid, was filtered and the filtrate evaporated *in vacuo*. The residue, *perhydro-11-methylphenanthrene*, distilled at 110—115°(bath)/0·05 mm. (0·35 g.) (Found : C, 87·3; H, 12·8. $C_{15}H_{26}$ requires C, 87·4; H, 12·6%). The product had a pleasant terpenoid odour, and there was no colouration with tetranitromethane.

Reduction of the enol acetate (0·4 g.) in ethanol (8 c.c.) in the presence of palladised strontium carbonate caused the absorption of hydrogen equivalent to H_2. The product (XXI) was hydrolysed by 7 hours' refluxing with aqueous 5N-potassium hydroxide (10 c.c.) and methanol (10 c.c.). Evaporation of the methanol and ether-extraction afforded Δ^4-dodecahydro-11-methyl-3-oxophenathrene, identical with an authentic specimen.

Δ^4-Dodecahydro-3-hydroxy-11-methylphenanthrene (XXII).—The Δ^4-ketone (1·0 g.) was added to a solution of aluminium *iso*propoxide (4 g.) in dry *iso*propyl alcohol (25 c.c.), and the mixture heated on the steam-bath, under an Allihn partial condenser, so that distillation occurred at the rate of about one drop every 5 sec. The distillate gave a negative Lund test for acetone after 1 hr. A further 10 c.c. of *iso*propyl alcohol was added and the mixture refluxed for 30 min., and then distilled for a further 30 min. Decomposition with ice and potassium hydroxide solution (20 c.c. of 20%) and ether-extraction gave the alcohol (1·0 g.) as a mixture of epimerides (cf. Schoenheimer and Evans, *J. Biol. Chem.*, 1936, **114**, 587).

$\Delta^{3:12}$-Decahydro-11-methylphenanthrene (XXIII).—A solution of the above epimeric alcohols (1·0 g.) in 95% ethanol (25 c.c.) containing two drops of concentrated hydrochloric acid was gently refluxed for 4 hr. The cooled solution was poured into a large volume of water, and the product isolated with ether. The *diene* distilled at 105°(bath)/0·08 mm. (0·7 g.) (Found : C, 88·8; H, 11·0. $C_{15}H_{22}$ requires C, 89·1; H, 10·9%). The product gave a brownish-yellow colour with tetranitromethane in chloroform, and showed maximum absorption in the ultraviolet region at 245 mμ (log ε 4·1).

Perhydro-3-hydroxy-11-methylphenanthrene (XXIV).—Sodium (4·0 g.) was added in small pieces to a gently refluxing solution of the Δ^4-ketone (0·5 g.) in dry pentyl alcohol (30 c.c.) during 1 hr. The solution was finally refluxed at 210—215° for 3½ hr. Ice was added, followed by water and ether. The ethereal layer was separated, dried, and evaporated. *Perhydro-3-hydroxy-11-methylphenanthrene* distilled at 140—145°(bath)/0·04 mm. (0·5 g.) (Found : C, 81·0; H, 11·5. $C_{15}H_{26}O$ requires C, 81·1; H, 11·7%). Oxidation of the product (0·5 g.) in acetic acid (8 c.c.) with chromic acid (0·25 g.) gave *perhydro-11-methyl-3-oxophenanthrene* (semicarbazone, m. p. and mixed m. p. 232°).

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THE DYSON PERRINS LABORATORY, OXFORD UNIVERSITY. [*Received, March 28th*, 1955.]

Experiments on the Synthesis of Substances Related to the Sterols. Part LIII. Stereospecific Synthesis of a Tricyclic Ketone.*

By J. W. Cornforth, O. Kauder, J. E. Pike, and Sir Robert Robinson.

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The first steps to improve the formal total synthesis of androgenic hormones and cholesterol described earlier involved studies of the *C*-methylation of appropriate naphthalene derivatives and of the hydrogenation of model substances as well as of the compounds actually required for the synthesis. First, for the preparation of 5-methoxy-1-methyl-2-tetralone, it was found advantageous to proceed from 5-acetamido-1-naphthol rather than from 1 : 6-dihydroxynaphthalene as heretofore. Next a procedure was devised which avoided an irksome demethylation.

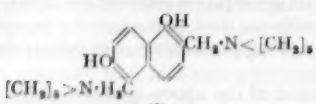
From this point a *cis*-A/B-ring was formerly set up largely as a matter of urgency to enable use to be made of the more accessible relay points.

A device for producing the *trans*-A/B-decalin system has now been successfully adopted and the new synthetic scheme has been taken as far as a tricyclic keto-ester in which only the asymmetric centre added last is of undetermined configuration.

In an earlier communication it was stated that the formal total syntheses recorded in this series (*J.*, **1946**, **676**; **1949**, **1855**; **1953**, **361**) should be regarded as scaffolding; the first steps in construction, within this framework, of a more seemly edifice are now reported.

The initial stages, before problems of stereoisomerism arose, were capable of improvement in several respects: in particular, it was desirable to improve or to circumvent the mono-*C*-methylation of 5-methoxy-2-tetralone. Many attempts to raise the yield in the process were made and one such is described in the Experimental section. The yield of crude product was about 50% in the best trials but even so the separations involved were tedious and the results not fully reproducible.

Hence we turned to the *C*-methylation of naphthalene derivatives by catalytic reduction of piperidinomethyl compounds. Unfortunately 1 : 6-dihydroxynaphthalene could not be converted into a mono(piperidinomethyl) derivative but always gave the disubstituted substance (I). This base could be converted into a diacetyl derivative by treatment with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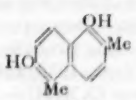
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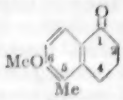
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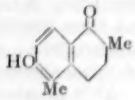

(IV)

acetyl chloride in cold acetone or into a tetra-acetate (replacement of piperidine groups by acetoxyl) by heating with acetic anhydride. It was catalytically reduced with palladised strontium carbonate or Raney nickel to 1 : 6-dihydroxy-2 : 5-dimethylnaphthalene (II). The constitution of this substance was proved by its synthesis from 6-methoxy-5-methyl-1-tetralone (III) (Martin and Robinson, *J.*, **1943**, **491**) by way of a 2-formyl derivative, *C*-methylation of this, hydrolysis, dehydrogenation, and demethylation.

After extensive study of the nuclear hydrogenation of piperidinomethylnaphthols, the base (I) was hydrogenated under pressure over W-7 Raney nickel in alcohol to a number of products, one of which proved to be 6-hydroxy-2 : 5-dimethyl-1-tetralone (IV). This could be methylated with formation of the 2-methyl derivative of (III), an intermediate in the above-mentioned synthesis of (II).

As we were unable to effect the mono-*C*-methylation of 1 : 6-dihydroxynaphthalene we turned to the use of the more readily available 5-acetamido-2-naphthol (V) as the starting material. Reaction with piperidine and formaldehyde gave the piperidinomethyl derivative (VI), which was reduced smoothly to 5-acetamido-1-methyl-2-naphthol

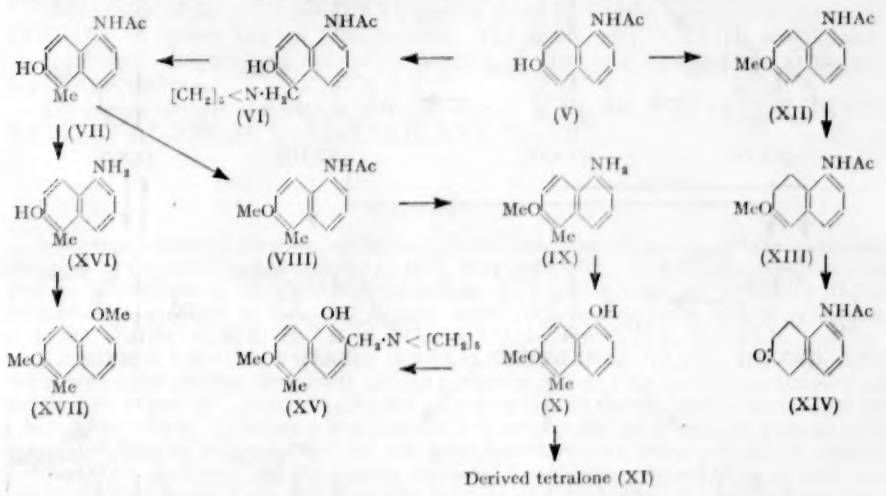
* Part LII, preceding paper.

(VII) by catalytic hydrogenation over palladium–strontium carbonate in the presence of oxalic acid. High temperature and pressure were unnecessary; thus the procedure is more convenient than the high-pressure hydrogenation which was used by Caldwell and Thompson (*J. Amer. Chem. Soc.*, **1939**, **61**, 765) for other dialkylaminomethylphenols and by us in earlier experiments.

Methylation of the naphthol (VII) was followed by hydrolysis to the amine (IX). The Bucherer reaction worked well with this amine, and afforded 6-methoxy-5-methyl-1-naphthol (X) in high yield. An alternative preparation of this naphthol, and its reduction by sodium in ethanol–liquid ammonia, followed by hydrolysis to the β-tetralone (XI), were reported in Part XLV (*loc. cit.*, 1946).

Some alternative routes from 5-acetamido-2-naphthol were investigated as possible variants of the preferred scheme indicated above.

Reduction of 1-acetamido-6-methoxynaphthalene (XII) by sodium in ethanol–liquid ammonia gave, by way of the enol ether (XIII), 5-acetamido-2-tetralone (XIV), though the yield was poor. Again, the naphthol (X) was treated with formaldehyde and piperidine to give the base (XV), with a view to early introduction of the future C/D angular methyl group. A third approach involved hydrolysis of the methylnaphthol (VII) and exchange of the amino-group in the product (XVI) for hydroxyl; methylation then gave 2 : 5-dimethoxy-1-methylnaphthalene (XVII). The reduction of this substance, in moderate yield, to 6-methoxy-5-methyl-2-tetralone was mentioned in an earlier paper; attempts to improve the yield by using a liquid ammonia medium were not successful.

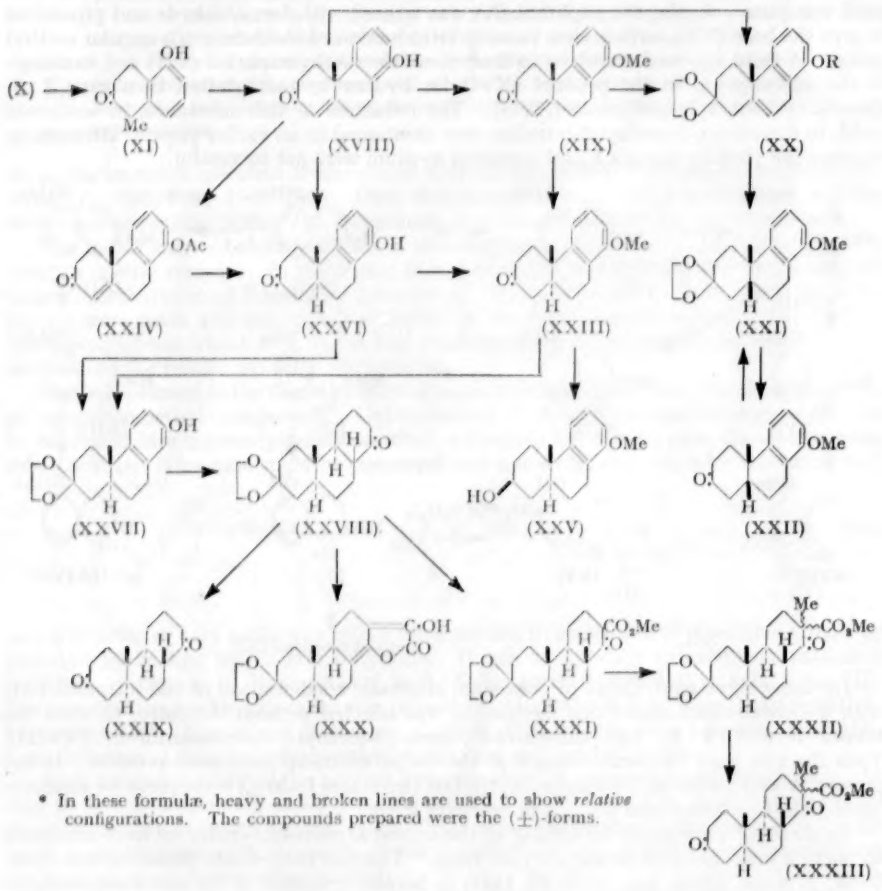


By using three equivalents of potassium ethoxide, condensation of the tetralone (XI) with 4-diethylaminobutan-2-one methiodide was effected without difficulty, to yield the known 5 : 6 : 7 : 9 : 10 : 13-hexahydro-1-hydroxy-13-methyl-7-oxophenanthrene (XVIII). Thus the two least favourable stages of the earlier synthesis have been avoided. In the present procedure the yields obtained in the last two stages (~50%) leave room for improvement; all the other stages proceed in excellent yield.

In choosing a procedure for setting up the second asymmetric centre we were concerned to make a *trans*-junction of the alicyclic rings. This has been shown (Renfrow and Cornforth, *J. Amer. Chem. Soc.*, **1953**, **75**, 1347) to favour formation of the *anti-trans*-configuration when the aromatic ring is hydrogenated, whereas a *cis*-junction favours the *syn-trans*-configuration. In the earlier synthesis we hydrogenated the double bond in the ketone (XVIII) catalytically, obtaining a *cis*-junction, and were certainly fortunate at the perhydrophenanthrene stage to obtain even a minor proportion of the desired *cis-anti-trans*-isomeride along with a much larger amount of *cis-syn-trans*-material.

The ketone (XVIII) and its methyl ether (XIX) were readily converted into the ethylene ketals (XX). The shift of the double bond is presumed by analogy with many known examples. Catalytic addition of hydrogen to this double bond in the ketal (XX; R = Me) occurred, unfortunately, on the β-side, the product (XXI) being identical with a ketal prepared from the known *cis*-methoxy-ketone (XXII), to which it could be hydrolysed by acid. Evidently the α-oxygen atom, in the ketal group, is able to force β-addition of hydrogen, as it does in *epi*cholesterol (Lewis and Shoppee, *Chem. and Ind.*, 1953, 897).

Reduction by dissolving metals usually produces the thermodynamically stable isomeride when more than one may theoretically be formed (for bibliography see Arth *et al.*, *J. Amer. Chem. Soc.*, 1954, **76**, 1717). When the methoxy-ketone (XIX) was reduced with lithium in liquid ammonia the *trans*-ketone (XXIII) was isolated in 65% yield, a better result than could be obtained (Renfrow and Cornforth, *loc. cit.*) by reduction with sodium and pentyl alcohol followed by re-oxidation. When the methoxy-ketone (XIX) was



* In these formulæ, heavy and broken lines are used to show *relative* configurations. The compounds prepared were the (±)-forms.

reduced with lithium and ethanol in ammonia, or when its hydro-derivative (XXIII) was reduced with lithium aluminium hydride, the β-alcohol (XXV) was formed; the acetate of this alcohol had already been reported (Renfrow and Cornforth, *loc. cit.*). Reduction of

the acetate (XXIV) of the phenolic ketone (XVIII) by lithium in liquid ammonia gave the *trans*-ketone (XXVI) in similar yield; the phenolic ketone (XVIII) itself gave a lower yield.

The keto-group was then protected before reduction of the aromatic ring. Treatment of the ketone (XXVI) with ethylene glycol gave the ketal (XXVII), which could also be prepared quite conveniently from the methoxy-ketone (XXIII) by reaction with ethylene glycol and demethylation with potassium hydroxide in methanol at 190°.

Hydrogenation of the phenolic ketal (XXVII) over W2 Raney nickel in alkaline ethanol, followed by oxidation of the total product with chromium trioxide–pyridine (Sarett *et al.*, *J. Amer. Chem. Soc.*, 1953, **75**, 422) afforded a good yield of the ketonic monoketal (XXVIII). The *trans-anti-trans*-configuration of this substance was checked by hydrolysis to the diketone (XXIX) which was proved by m. p., mixed m. p., and infrared spectrum to be identical with the ketone previously prepared (Renfrow and Cornforth, *loc. cit.*) and correlated with the Köster–Logemann ketone derived from cholesterol. Thus four of the six asymmetric centres determining configuration of the steroid ring system had been set up in correct relation by a stereospecific procedure.

Reaction of the diketone monoketal (XXVIII) with sodium hydride and methyl carbonate led smoothly to the keto-ester (XXXI). An attempt to make this keto-ester *via* the glyoxylate gave a somewhat surprising result: reaction of the ketal ketone (XXVIII) with methyl oxalate and sodium methoxide in benzene afforded, as the sole crystalline product, the enol lactone (XXX), characterised as its methyl ether.

Methylation of the keto-ester (XXXI) gave in about 70% yield, a single stereoisomeride (XXXII); no epimer has yet been isolated. The diketo-ester (XXXIII) was obtained on hydrolysis. Experiments are now in progress to determine configuration at the new asymmetric centre.

The preferred route of syntheses is by the stages; V, VI, VII, VIII, IX, X, XI, XVIII, XXVI, XXVII, XXVIII, XXXI, XXXII, XXXIII.

Experimental

5-Methoxy-1-methyl-2-tetralone.—5-Methoxy-2-tetralone was prepared by the procedure described by Cornforth and Robinson (*J.*, 1942, 689; 1946, 676). 1 : 6-Dihydroxynaphthalene (200 g.) afforded 125 g. (57%) of distilled ketone, m. p. 33—35° (lit., m. p. 36—37°). The *semicarbazone*, prepared in the usual manner, crystallised from aqueous ethanol in needles, m. p. 165° (Found: C, 57·6; H, 7·0. $C_{12}H_{15}O_2N_3,H_2O$ requires C, 57·3; H, 6·8%).

A solution of 5-methoxy-2-tetralone (3·5 g.) in light petroleum (75 c.c.; b. p. 100—120°) was stirred under nitrogen with finely divided potassium (0·8 g.) for 4 hr. at room temperature and for ½ hr. at 65—70°. Methyl iodide (5·6 g.) was added and the temperature maintained for ½ hr. After cooling, the mixture was acidified and evaporated under reduced pressure; the mixture of ketones was separated by the usual procedure with sodium hydrogen sulphite (Cornforth and Robinson, *loc. cit.*), giving recovered 5-methoxytetralone (0·4 g.), 5-methoxy-1-methyl-2-tetralone (1·8 g.), and a residue containing 5-methoxy-1 : 1-dimethyl-2-tetralone (0·1 g.).

The crude monomethylated ketone from a number of runs was shaken in ether with saturated sodium hydrogen sulphite solution and distilled. The product, b. p. 127—129°/0·8 mm., solidified and formed colourless, elongated prisms, m. p. 46—47°.

This material (6·9 g.) gave 6·5 g. of 5 : 6 : 7 : 9 : 10 : 13-hexahydro-1-methoxy-13-methyl-7-oxophenanthrene which, on crystallisation from ether (yield, 4·3 g.), had m. p. 112—114°. Cornforth and Robinson (*loc. cit.*) give m. p. 115—116° for the pure substance.

1 : 6-Dihydroxy-2 : 5-bispiperidinomethylnaphthalene (I).—Technical dihydroxynaphthalene was recrystallised from benzene by a Soxhlet extraction procedure (recovery 92%) and distilled at 260—270°(bath)/0·1 mm. A mixture of aqueous formaldehyde (7·5 c.c. of 40%) in ethanol (15 c.c.) was added with gentle agitation under nitrogen to a solution of 1 : 6-dihydroxynaphthalene (8·0 g.) and piperidine (10·2 g.) in ethanol (40 c.c.), kept at 15—20°. Deposition of crystals began after ½ hr. at room temperature. The product (14·6 g.), washed with methanol and dried at room temperature, consisted of colourless plates, m. p. 133°, unchanged by recrystallisation from ethanol or *cyclo*hexane (Found: C, 74·8; H, 8·3; N, 8·1. $C_{22}H_{30}O_2N_2$ requires C, 74·5;

H, 8·5; N, 7·9%). The *base* is photosensitive, and slowly decomposed by heat, acid, or alkali into piperidine and a yellow to brown polymer which does not contain nitrogen. It was unaffected by diazomethane in ether–methanol. Its *OO-diacetyl derivative* was obtained when acetyl chloride (2 c.c.) was added to a solution of the base (1 g.) in acetone (15 c.c.). The precipitate was washed with ether, covered with ether, and treated with a saturated solution of sodium hydrogen carbonate. The diacetate, obtained from the ethereal layer, crystallised from light petroleum (b. p. 80—100°) as colourless prisms, m. p. 118—119° (Found: C, 71·5; H, 7·5. $C_{26}H_{34}O_4N_2$ requires C, 71·2; H, 7·8%).

A mixture of the base (I) (1 g.) and acetic anhydride (8 c.c.) was heated on the steam-bath for 3 hr. Enough water was added to give a clear solution on warming; this was treated with charcoal, filtered, and chilled. 1 : 6-*Diacetoxy*-2 : 5-*bisacetoxymethylnaphthalene* (0·6 g.) was obtained as prisms, m. p. 82—83°, after crystallisation from aqueous methanol (1 : 1) (Found: C, 61·6; H, 5·3. $C_{20}H_{20}O_8$ requires C, 61·8; H, 5·2%).

1 : 6-*Dihydroxy*-2 : 5-*dimethylnaphthalene* (II).—(*a*) Attempted hydrogenation of the base (I) using a copper–chromium oxide catalyst at 165° gave only piperidine and polymeric decomposition products.

(*b*) A mixture of the base (3 g.), 2% palladised strontium carbonate (1·5 g.), and ethanol (90 c.c.) was shaken with hydrogen at atmospheric pressure. Absorption of the gas was slow and stopped after slightly more than two equivalents had been taken up in 15 hr. Addition of fresh catalyst after 5 and 10 hr. failed to accelerate the process. The residue after removal of catalyst and solvent was taken up in ether and washed with dilute hydrochloric acid, causing the separation of much tar. Evaporation of the dried ethereal solution left a reddish, semi-crystalline mass from which no crystalline product could be isolated. It was accordingly methylated by means of methyl sulphate and aqueous sodium hydroxide. The crude product (0·4 g.) had m. p. 81—84°. Two crystallisations from methanol gave 1 : 6-*dimethoxy*-2 : 5-*dimethylnaphthalene* as cream-coloured plates, m. p. 88° (Found: 78·0; H, 7·6. $C_{14}H_{16}O_2$ requires C, 77·7; H, 7·5%).

(*c*) Similarly, when the base (2 g.) in ethanol (60 c.c.) was shaken with fresh W-7 Raney nickel and hydrogen at 45 lb./sq. in. absorption stopped after 22 hr. The product was isolated as above, and again methylated directly to give the dimethyl ether (0·3 g.).

(*d*) The base (3·5 g.) with oxalic acid (1·8 g.) in aqueous methanol (70 c.c. of 50%) was hydrogenated over palladised strontium carbonate (3 g.) at the ordinary temperature and pressure. Absorption of hydrogen stopped after slightly more than half of the theoretical amount had been taken up; addition of more catalyst led to no further absorption. The filtrate and washings from the catalyst were concentrated at 30—40° under reduced pressure, and diluted with water; the microcrystalline precipitate (0·7 g.) was twice crystallised from 35% aqueous methanol, to give 1 : 6-*dihydroxy*-2 : 5-*dimethylnaphthalene* as cream-coloured prisms, m. p. 127—129° (Found: C, 76·2; H, 6·2. $C_{12}H_{12}O_2$ requires C, 76·6; H, 6·4%). Some unreduced base (0·5 g.) was recovered from the filtrate by addition of aqueous ammonia. The dihydric phenol gave an orange colour with diazobenzenesulphonic acid, changed to deep purple by addition of alkali. It developed a light colour in very dilute solution with 2 : 6-dichloroquinone *N*-chloroimide. The ferric reaction was negative. Methylation gave the dimethyl ether, m. p. 87—88°.

2-*Formyl*-6-*methoxy*-2 : 5-*dimethyl*-1-*tetralone*.—A solution of 2-hydroxymethylene-6-methoxy-5-methyl-1-tetralone (E. B. Smith, D.Phil. Thesis, Oxford, 1949) (3·7 g.) and methyl iodide (4·5 g.) in acetone (25 c.c.) was heated on the steam-bath with freshly ignited, powdered potassium carbonate (2·5 g.); more methyl iodide (2 g.) and acetone (10 c.c.) were added after 15 hr. After 21 hr. the ferric reaction was negative. Dry ether (25 c.c.) was added to the cooled solution, which was filtered and evaporated, leaving a solid residue. (On addition of 2 drops of alcoholic ferric chloride a methanolic solution of this material slowly developed a green colour, indicating the presence of a small proportion of the *O*-methyl derivative.) Two crystallisations from light petroleum (b. p. 60—80°) gave colourless plates of the *keto-aldehyde*, m. p. 52—54° (Found: C, 72·6; H, 7·1. $C_{14}H_{16}O_3$ requires C, 72·4; H, 6·9%).

6-*Methoxy*-2 : 5-*dimethyl*-1-*tetralone*.—The entire crude formylmethoxydimethyltetralone, obtained as last described, was kept for ½ hr. with a solution of hydrochloric acid (3 c.c.) in 50% aqueous methanol (17 c.c.). The mixture was basified with 5% potassium hydroxide solution (100 c.c.) and extracted with ether. Acidification of the aqueous layer gave recovered hydroxymethylenemethoxymethyltetralone (0·4 g.), presumably formed by hydrolysis of its *O*-methyl derivative. The residue left after evaporation of the ethereal layer was heated for 10 min. with a solution of potassium hydroxide (3 g.) in methanol (30 c.c.). Addition of dilute

hydrochloric acid to the cooled solution precipitated the methylated tetralone (2·3 g.). Distillation of the crude ketone, b. p. 175—180° (air-bath)/0·1 mm., and crystallisation from 80% aqueous methanol gave colourless plates or needles, m. p. 114—115°. Martin and Robinson (*loc. cit.*, p. 494, line 51) give m. p. 113°. The dark red 2 : 4-dinitrophenylhydrazone had m. p. 226—229° (lit., 229°).

6-*Methoxy*-2 : 5-*dimethyl*-1-*naphthol*.—The tetralone (2 g.) was heated with sulphur (0·25 g., 75% of the theoretical amount) at 220—225° for 1·5 hr. A boiling benzene extract (charcoal) of the product was filtered, and extracted with three portions of 5% sodium hydroxide solution. Acidification of the combined alkaline extracts precipitated the *naphthol*. Two crystallisations from light petroleum (b. p. 60—80°) gave clusters of yellowish prisms, m. p. 79—80° (Found : C, 77·0; H, 6·9. $C_{13}H_{14}O_2$ requires C, 77·2; H, 7·0%).

1 : 6-*Dimethoxy*-2 : 5-*dimethylnaphthalene*.—The above naphthol was recovered unchanged after being kept overnight with an excess of ethereal diazomethane. The naphthol (0·4 g.) was methylated with methyl sulphate (1 c.c.) and 10% sodium hydroxide (5 c.c.) in the usual way. The product (0·4 g.) solidified on cooling, and after two crystallisations from 90% aqueous methanol had m. p. 87—88°, alone or mixed with a specimen from the successive hydrogenation and methylation of the base (I).

Hydrogenation of 2-*Methoxy*-1-*naphthaldehyde*.—The aldehyde was prepared from 2-methoxynaphthalene, *N*-methylformanilide, and phosphoryl chloride (cf. Wood and Bost, *Org. Synth.*, 1940, **20**, 11). The crude product was crystallised from ethanol (charcoal) and recrystallised from aqueous ethanol, to give colourless needles or plates, both forms melting at 84—85° and being interconvertible by seeding. The needles change into plates on prolonged contact with the saturated solution. From the mother-liquors, more aldehyde was obtained by evaporation and steam-distillation (total yield, 77%).

The aldehyde (20 g.), ethanol (60 c.c.), acetic acid (1 c.c.), and Raney nickel (2 g.) were heated and stirred with hydrogen at 100 atm. (cold). Four equiv. of hydrogen were taken up in 3½ hr. at 110°. The residue after removal of catalyst and solvent was mixed with twice its volume of methanol, and crystallised in the cold overnight. More crystals were obtained by cooling the mother-liquors to −60°. This product (8·8 g., 47%) was identified as 5 : 6 : 7 : 8-tetrahydro-2-methoxy-1-methylnaphthalene by its m. p. 50—51°, alone or mixed with an authentic specimen, and by oxidation to the tetralone, m. p. 112—113°.

The residue obtained by evaporation of the mother-liquors was steam-distilled and the volatile oil (5 g., 27%) had b. p. 85—86°/0·2 mm., n_D^{20} 1·5408. It was probably 1 : 2 : 3 : 4-*tetrahydro*-2-*methoxy*-1-*methylnaphthalene* (Found : C, 81·9; H, 8·9. $C_{12}H_{16}O$ requires C, 81·8; H, 9·2%.

The non-volatile residue from the steam-distillation solidified, and crystallised from light petroleum (b. p. 40—60°) or from water in colourless needles, or squat rhomboids, both of m. p. 67—68° and interconvertible by seeding. The needles changed into rhomboids in contact with the saturated solution. The product (2·2 g., 11%) reacted with acetyl chloride and dimethylaniline to give an oil which gave a positive hydroxamic acid test, and was therefore considered to be 5 : 6 : 7 : 8-*tetrahydro*-1-*hydroxymethyl*-2-*methoxynaphthalene* (Found : C, 74·9; H, 8·6. $C_{12}H_{16}O_2$ requires C, 75·0; H, 8·4%). Confirmation of the structure of this substance was obtained by synthesis.

5 : 6 : 7 : 8-*Tetrahydro*-2-*methoxy*-1-*naphthaldehyde*.—5 : 6 : 7 : 8-Tetrahydro-2-naphthol (3·5 g.; m. p. 60—61°) was converted into 5 : 6 : 7 : 8-tetrahydro-2-hydroxy-1-naphthaldehyde by the Reimer–Tiemann reaction following the procedure described by Arnold, Zaugg, and Sprung (*J. Amer. Chem. Soc.*, 1941, **63**, 1314). The product (0·9 g.), colourless plates from 35% aqueous ethanol, had m. p. 83—84° (lit., 86°).

The hydroxy-aldehyde was methylated with methyl sulphate and sodium hydroxide solution, and the *methoxy-aldehyde* crystallised from methanol as long, thin, colourless prisms, m. p. 63—64° (Found : C, 75·1; H, 7·8. $C_{12}H_{14}O_2$ requires C, 75·7; H, 7·4%). The substance is photosensitive.

5 : 6 : 7 : 8-*Tetrahydro*-1-*hydroxymethyl*-2-*methoxynaphthalene*.—4M-Ethereal lithium aluminium hydride (1 c.c.) was added to a solution of the above methoxy-aldehyde (25 mg.) in ether (10 c.c.). Excess of the hydride was decomposed by moist ether and dilute hydrochloric acid. The ethereal layer was washed with water, dried ($MgSO_4$), and evaporated, leaving the alcohol as a crystalline residue. After recrystallisation from water, this had m. p. 67—68°, alone or mixed with a specimen from the hydrogenation of 2-methoxy-1-naphthaldehyde.

Hydrogenation of Mannich Bases from β-*Naphthol*.—(*a*) 1-Piperidinomethyl-2-naphthol (12 g.; m. p. 96°) in ethanol (60 c.c.) was hydrogenated over copper–chromium oxide catalyst

(1·5 g.) at 160°/90 atm. (cold). Absorption of hydrogen was slow after 3 hr., and was then stopped. Removal of catalyst and solvent left a pale yellow oil. This was dissolved in benzene and extracted successively with dilute hydrochloric acid, water, and three portions of 10% sodium hydroxide solution. No starting material was found in the acid extract. Acidification of the alkaline extracts gave crude 1-methyl-2-naphthol (2·6 g.); crystallisation from water gave small felted needles, m. p. and mixed m. p. 110—111°.

The neutral material left by evaporation of the benzene was distilled, giving a colourless oil (4·3 g., b. p. 101—102°/0·1 mm., n_D^{20} 1·5587) which is probably 1 : 2 : 3 : 4-tetrahydro-1-methyl-2-naphthol. McKusick (*J. Amer. Chem. Soc.*, 1948, **70**, 2196) gives b. p. 105—107°/0·2 mm., n_D^{25} 1·5570.

(*b*) The above base (3 g.) in ethanol (50 c.c.) was hydrogenated over palladised strontium carbonate at the ordinary temperature and pressure, one equiv. of hydrogen being taken up in 1½ hr. 1-Methyl-2-naphthol (1·55 g., 77%) was isolated as described above.

(*c*) The base (4 g.) in ethanol (60 c.c.) was hydrogenated over fresh W-7 Raney nickel in the Burgess–Parr apparatus. No hydrogenation occurred at a pressure of less than 35 lb./sq. in., but when that pressure was maintained the hydrogenation was complete in 3 hr., giving 1-methyl-2-naphthol (1·8 g., 67%) isolated as before. The need for a certain minimum hydrogen pressure in the use of W-7 Raney nickel was also observed with other phenolic bases, as well as in the reduction of benzyl alcohol and acetophenone to hydrocarbons, but not in the hydrogenation of *cyclo*hexene or cinnamic acid.

(*d*) 1-Dimethylaminomethyl-2-naphthol (40·2 g.; m. p. 74°) in ethanol (80 c.c.) was hydrogenated over W-7 Raney nickel at 50—60°/100 atm. (cold). Absorption of hydrogen was stopped after the drop in pressure corresponded to approximately 1 equiv. (1 hr.). Isolation by the usual procedure gave 1-methyl-2-naphthol (23·1 g., 73%) and some neutral material (6 g., not investigated).

(*e*) The same base (20 g.) in ethanol (75 c.c.) was hydrogenated at 80—100°/100 atm. (cold) with an aged specimen of W-7 Raney nickel. The pressure remained constant after the absorption of about 3 equiv. (6 hr.). Isolation as described above gave only a trace of phenolic material together with an apparently neutral oil (13 g., b. p. 100—102°/0·1 mm., n_D^{20} 1·5605). The distillate deposited some long needles in the cold, but it was not possible to remove adhering oil without melting the crystals; some of the oil removed had n_D^{20} 1·5595. When the hydrogenation was repeated on five times the scale, the product was worked up in the manner described for the isolation of 1 : 2 : 3 : 4-tetrahydro-2-naphthol (Dauben, McKusick, and Muller, *J. Amer. Chem. Soc.*, 1948, **70**, 4170). A benzene solution of the product was washed with 10% sodium hydroxide solution (3 × 30 c.c.) (the alkaline extracts yield only 2 g. of phenolic product), evaporated, and distilled. The product, b. p. 102°/0·1 mm., n_D^{20} 1·5583 (55 g., 66%), was probably 1 : 2 : 3 : 4-tetrahydro-1-methyl-2-naphthol (Found: C, 81·4; H, 9·0. Calc. for $C_{11}H_{14}O$: C, 80·8; H, 8·7%). The residue from the distillation was dissolved in warm 20% sodium hydroxide solution, clarified with charcoal, and acidified, giving 5 : 6 : 7 : 8-tetrahydro-1-methyl-2-naphthol (15 g., 18%), which crystallised from light petroleum (b. p. 60—80°) in colourless needles, m. p. and mixed m. p. 113°.

(*f*) Acetic acid (7 g.) was added before a hydrogenation carried out as under (*e*). After the uptake of three equiv. of hydrogen, the phenolic product (6·5 g.) and a neutral oil (7 g.) were isolated. After this process had been repeated with five times the given quantities, the solvent-free reaction product and 20% sodium hydroxide solution were distilled with steam. Acidification of the alkaline solution gave the phenol (39·5 g., 46%). The neutral isomeride (28 g., 35%) was isolated from the distillate.

1-*Acetoxymethyl-2-naphthyl Acetate*.—1-Dimethylaminomethyl-2-naphthol (3 g.) and acetic anhydride (21 c.c.) were heated on the steam-bath for 3 hr. Enough water was added to give a clear solution on warming. The colourless *diacetate* (3·5 g.) crystallised on cooling; recrystallisation from 60% aqueous methanol gave square plates, m. p. 76° (Found: C, 69·8; H, 5·6. $C_{15}H_{14}O_4$ requires C, 69·8; H, 5·5%).

Hydrogenation. (*a*) The diacetate (2·8 g.) was hydrogenated in ethanol over 10% palladised charcoal (1 g.) at room temperature and pressure. One equiv. of hydrogen was taken up in 1½ hr. Methanolic 2N-potassium hydroxide (15 c.c.) was added to the filtrate from the catalyst, and the solution was heated on the steam-bath for 15 min. After removal of the solvent, water (15 c.c.) and dilute hydrochloric acid (30 c.c.) were added, giving 1-methyl-2-naphthol (1 g., 66%), m. p. 109—111°.

(*b*) The diacetate (14 g.) in methanol (85 c.c.) was hydrogenated over W-7 Raney nickel (3 g., aged six weeks) at 80—95°/90 atm. (cold), until the pressure drop corresponded to three

equiv. of hydrogen. Alkaline hydrolysis, evaporation, and acidification gave an oil, which was taken up in benzene, and extracted with dilute alkali; acidification gave the phenolic 5-methyl-6-hydroxytetralin (3·6 g., 64%). Evaporation of the benzene left an oil, presumably containing the non-phenolic isomeride (1 g., 18%).

Perhydrogenation Experiments.—(*a*) 1-Piperidinomethyl-2-naphthol (6 g.) in ethanol (50 c.c.) was hydrogenated over fresh W-7 Raney nickel. Absorption of approx. 6 equivs. of hydrogen was complete after 7 hr. at 100—110°/*ca.* 100 atm. (cold). Removal of catalyst and solvent left a colourless oil (3·8 g.). This material, in acetic acid (40 c.c.), was oxidised at 15—20° by the dropwise addition of chromic anhydride (4 g.) in water (4 c.c.) and acetic acid (36 c.c.). The excess of chromic acid was decomposed with sodium hydrogen sulphite solution, and most of the acetic acid removed by concentration under reduced pressure. The ketone, isolated by means of ether, was obtained as a colourless oil (2·7 g.). After this product had been heated with methanolic potassium hydroxide (50 c.c.) for 4 hr., derivatives were prepared. The 2 : 4-dinitrophenylhydrazone had m. p. 169—170° after two crystallisations from ethanol–ethyl acetate. The semicarbazone had m. p. 206—208° (decomp.) after three crystallisations from aqueous ethanol. These melting points were not depressed on admixture with authentic specimens of the derivatives of *trans*-1-methyl-2-decalone.

(*b*) Essentially the same procedure was applied to 2-piperidinomethyl-1-naphthol. After homogenisation with boiling methanolic potassium hydroxide solution as above, the ketone obtained gave a semicarbazone, m. p. 218—220° (decomp.) (from aqueous ethanol), and a 2 : 4-dinitrophenylhydrazone, m. p. 237—238° (from ethanol–benzene), undepressed on admixture with authentic specimens of the respective derivative of *trans*-2-methyl-1-decalone.

(*c*) The base (I) (7 g.) in ethanol (90 c.c.) was hydrogenated over fresh W-7 Raney nickel at 90—105°/110 atm. (cold). Absorption of hydrogen corresponded to about 7 equiv. and stopped after 2 hr. After removal of catalyst and solvent the gummy product was extracted with cold dilute hydrochloric acid and then with ether; evaporation of the ether and evaporative distillation gave two fractions: (i) a viscous colourless liquid, b. p. (bath) 90—100°/0·001 mm. (Found: C, 78·3; H, 8·5%), and (ii) a light yellow, gummy solid which reddened on exposure to air and had b. p. *ca.* 115°/0·001 mm. (Found: C, 76·0; H, 8·1%); the analyses indicated that in spite of the pressure hydrogenation had been incomplete. Both fractions were therefore dissolved in ether and extracted with 10% sodium hydroxide solution. The solid precipitate obtained on acidification of the aqueous layer (2·9 g.) was distilled; the distillate (b. p. *ca.* 120°/0·002 mm., slight decomp.) solidified and had m. p. 175—180°. Crystallisation from 35% aqueous methanol, sublimation at 130°/0·02 mm., and recrystallisation from 35% methanol gave slender yellow prisms, m. p. 180—182° (Found: C, 75·7; H, 7·5. $C_{12}H_{14}O_2$ requires C, 75·7; H, 7·4%). Methylation of the product with methyl sulphate and alkali gave a methyl ether, m. p. 114—115°, which was identified as 6-methoxy-2 : 5-dimethyl-1-tetralone by direct comparison and by preparation of the 2 : 4-dinitrophenylhydrazone, m. p. 227—229°. The phenolic ketone was therefore 6-*hydroxy*-2 : 5-*dimethyl*-1-*tetralone* (IV).

The 2 : 4-*dinitrophenylhydrazone*, needles from ethanol–ethyl acetate, had m. p. 260—263° (decomp.) (Found: C, 58·0; H, 5·1. $C_{18}H_{18}O_5N_4$ requires C, 58·4; H, 4·9%). The action of boiling acetic anhydride and pyridine gave the *acetoxy-ketone*, colourless prisms (from 80% aqueous methanol), m. p. 78—79° (Found: C, 72·1; H, 7·0. $C_{14}H_{16}O_3$ requires C, 72·4; H, 6·9%). Benzylation was accomplished by heating the phenolic ketone, benzyl chloride, and potassium carbonate in acetone until the diazo-coupling reaction was negative; after absorption on alumina and elution with benzene–light petroleum (1 : 1), the *benzyloxy-ketone* crystallised from light petroleum (b. p. 60—80°) as colourless prisms, m. p. 102—103° (Found: C, 81·4; H, 7·4. $C_{19}H_{20}O_3$ requires C, 81·4; H, 7·2%).

Evaporation of the ethereal solution from which the phenolic ketone had been extracted left a small amount of residue, the amount of which varied with the temperature at which the hydrogenation had been conducted. No residue was obtained from reactions at 100° or below. In one run the temperature was allowed to reach 160°; the residue then obtained (0·6 g.) was a mixture of oil and needles. Some of the needles were separated mechanically, washed with light petroleum (b. p. 40—60°), and recrystallised from this solvent. The product, m. p. 95—96°, was probably 5 : 6 : 7 : 8-*tetrahydro*-1 : 6-*dimethyl*-2-*naphthol* (Found: C, 82·3; H, 9·5. $C_{12}H_{16}O$ requires C, 81·8; H, 9·1%). The remaining product was stirred with four small portions of cold methanol, which dissolved the needles and some of the oil. The gummy residue solidified on being rubbed with cold methanol, and crystallisation from this solvent afforded small, squat prisms. This material, m. p. 105—107°, was probably 1 : 2 : 3 : 4-*tetrahydro*-1 : 6-*dihydroxy*-2 : 5-*dimethylnaphthalene* (Found: C, 74·4; H, 8·7. $C_{12}H_{16}O_2$ requires C, 75·0; H, 8·4%).

(*d*) 1 : 6-Dihydroxynaphthalene (8 g.) in ethyl acetate (100 c.c.) was hydrogenated over palladised strontium carbonate (5 g.) at 175°/92 atm. (cold) for 8 hr. Removal of catalyst and solvent left a solid residue (6·2 g.). Two crystallisations from 20% aqueous methanol gave light tan prisms (3·9 g.), m. p. 149—152°, which is the m. p. of 6-hydroxy-1-tetralone. Methylation in the usual way gave 6-methoxy-1-tetralone, m. p. and mixed m. p. 75—77°.

5-Acetamido-1-piperidinomethyl-2-naphthol (VI).—Commercial 5-acetamido-2-naphthol was purified by extraction in a Soxhlet apparatus with water and recrystallisation from aqueous ethanol (charcoal); then it was obtained as colourless needles, m. p. 217°.

Formaldehyde (60 c.c. of 40% solution) was added to a mixture of piperidine (90 c.c.) and 5-acetamido-2-naphthol (150 g.) in ethanol (1500 c.c.). Crystallisation began after ½ hr. and was complete after 12 hr. at room temperature. The crude product (185 g., 83%) was collected, washed with a little ethanol, and dried. Purification (which was necessary for the next stage) was effected by crystallisation from pentyl alcohol (charcoal); the base (152 g.) separated as colourless plates, m. p. 198° (Found: C, 72·8; H, 7·3; N, 8·9. $C_{18}H_{22}O_2N_2$ requires C, 72·4; H, 7·4; N, 9·4%).

Substitution of dimethylamine for piperidine in this procedure gave the *dimethylamino-analogue* in 37% yield, colourless prisms (from ethanol), m. p. 193—194° (decomp.) (Found: C, 70·3; H, 7·5; N, 10·2. $C_{15}H_{18}O_2N_2$ requires C, 69·8; H, 7·0; N, 10·8%).

A mixture of the piperidino-base (1 g.) and acetic anhydride (8 c.c.) was heated on the steam-bath for 3 hr. Enough water was added to give a clear solution on warming. On cooling, the product separated as an oil, which later solidified. Crystallisation from 50% aqueous ethanol gave colourless clustered prisms, m. p. 170—171°, consisting of *5-acetamido-1-acetoxymethyl-2-naphthyl acetate* (Found: C, 64·6; H, 5·8; N, 4·6. $C_{17}H_{17}O_5N$ requires C, 63·8; H, 5·4; N, 4·4%).

5-Acetamido-1-methyl-2-naphthol (VII).—5-Acetamido-1-piperidinomethyl-2-naphthol (30 g.) in aqueous methanol (600 c.c.; 1 : 1) containing oxalic acid (9·0 g.) was hydrogenated over 1% palladised strontium carbonate (20 g.) at *ca.* 40°/1 atm. Uptake of hydrogen was complete after 3 hr. The catalyst was removed and extracted with methanol (*ca.* 250 c.c.). Methanol was removed from the combined filtrates under reduced pressure, and 2N-hydrochloric acid (50 c.c.) added to the cooled solution. The precipitated solid was collected, washed with water, and dried, giving 5-acetamido-1-methyl-2-naphthol (19·4 g., 90%). It crystallised from aqueous ethanol as colourless needles, m. p. 195—196° (Found: C, 72·1; H, 5·6; N, 6·7. $C_{13}H_{13}O_2N$ requires C, 72·5; H, 6·1; N, 6·9%).

5-Amino-1-methyl-2-naphthol (XVI).—5-Acetamido-1-methyl-2-naphthol (23·7 g.), concentrated hydrochloric acid (100 c.c.), water (20 c.c.), and ethanol (50 c.c.) were refluxed for 3 hr. The solution was cooled and the hydrochloride decomposed with ammonia, to give *5-amino-1-methyl-2-naphthol* (17·5 g., 92%), which separated from aqueous ethanol (charcoal) in pale yellow needles, m. p. 186—187° (Found: C, 76·2; H, 6·5; N, 7·8. $C_{11}H_{11}ON$ requires C, 76·3; H, 6·4; N, 8·1%). The *dibenzoyl derivative* crystallised from ethanol in colourless needles, m. p. 231—232° (Found: C, 78·5; H, 5·0. $C_{25}H_{19}O_3N$ requires C, 78·7; H, 5·0%).

1 : 6-*Dihydroxynaphthalene*.—5-Acetamido-2-naphthol (21 g.) was refluxed with concentrated hydrochloric acid (90 c.c.), water (30 c.c.), and ethanol (75 c.c.) for 3 hr. After cooling, an excess of ammonia was added. The product (145 g., 87%), crystallised from aqueous ethanol (charcoal), gave 5-amino-2-naphthol as colourless needles, m. p. 189—190° (Brown, Hebden, and Withrow, *J. Amer. Chem. Soc.*, 1929, **51**, 1767, give m. p. 190°).

5-Amino-2-naphthol (10 g., 1 mol.) was stirred with freshly prepared 40% sodium hydrogen sulphite solution (130 c.c.) at about 95° for 15 hr., by which time a homogeneous solution had been obtained. Sodium hydroxide (50 g.) in water (40 c.c.) was added and the mixture boiled until no more ammonia was evolved (2 hr.). An excess of concentrated hydrochloric acid was cautiously added to the cooled solution, and the whole boiled until no more sulphur dioxide was evolved (1 hr.). 1 : 6-Dihydroxynaphthalene, which separated on cooling, was collected and dried (7·1 g., 70%). Recrystallisation from benzene gave colourless prisms, m. p. 137—138° (Fischer and Bauer, *J. prakt. Chem.*, 1916, **94**, 1, gave m. p. 137—138°). On the addition of ferric chloride to an aqueous solution a pale blue colour was developed, followed by a brownish-red precipitate.

2 : *5-Dihydroxy-1-methylnaphthalene*.—A mixture of 5-amino-1-methyl-2-naphthol (34·7 g.) and freshly prepared 40% sodium hydrogen sulphite solution (500 c.c.) was heated at 95° under reflux with vigorous stirring, for 16 hr. Aqueous sodium hydroxide (150 c.c. of 50%) was then added and the whole heated until the evolution of ammonia had ceased (3 hr.). After cooling, an excess of concentrated hydrochloric acid was cautiously added, and the mixture then boiled

for a further 2 hr. On cooling, **2 : 5-*dihydroxy*-1-*methylnaphthalene*** (30 g., 85%) separated; it crystallised from water (charcoal) as colourless needles, m. p. 163—164° (Found : C, 75·5; H, 5·7. $C_{11}H_{10}O_2$ requires C, 75·8; H, 5·7%).

A white precipitate was obtained on the addition of ferric chloride to a solution of this substance. A solution of 2 : 5-dihydroxy-1-methylnaphthalene (28 g.) in 2N-sodium hydroxide (250 c.c.) was shaken with methyl sulphate (25 c.c.) with intermittent gentle heating on the steam-bath. When the initial reaction had subsided, more 2N-sodium hydroxide (100 c.c.) and methyl sulphate (10 c.c.) were added. After further shaking, the mixture was kept for 2 hr., and the excess of methyl sulphate decomposed by heating on the steam-bath for ½ hr. The cooled solution was acidified, and extracted twice with chloroform. The combined extracts were washed with aqueous sodium hydroxide and with water, and then dried, and the solvent was removed, to yield 2 : 5-dimethoxy-1-methylnaphthalene (XVII) (22 g., 68%). After two crystallisations from ethanol it formed colourless, hexagonal plates, m. p. 84—85° (Cornforth and Robinson, *loc. cit.*, gave m. p. 85°). Purification was best effected by passing a solution of the crude product (11·7 g.) in light petroleum (b. p. 60—80°)–benzene (200 c.c. ; 2 : 1) through an alumina column ; colourless 2 : 5-dimethoxy-1-methylnaphthalene (11·0 g.), m. p. 84—85°, was obtained.

5-Acetamido-2-tetralone (XIV).—5-Acetamido-2-naphthol was methylated in the usual manner, with 2N-sodium hydroxide and methyl sulphate. Recrystallisation of the resulting methyl ether from ethanol gave 5-acetamido-2-methoxynaphthalene as colourless needles, m. p. 143—144° (Sachs, *Ber.*, 1906, **39**, 3016, gives m. p. 140°). Sodium (5 g.) was rapidly added to a mixture of 5-acetamido-2-methoxynaphthalene (9·6 g.), methanol (30 c.c.), ether (30 c.c.), and liquid ammonia (200 c.c.). Solvents were removed at about 50° and water (200 c.c.) was added, the product being precipitated. Re-acetylation was effected by dissolution of this material in pyridine (10 c.c.) and addition of acetic anhydride (3 c.c.). The whole was kept overnight at room temperature and poured into water, to give ***5-acetamido*-3 : 4-*dihydro*-2-*methoxynaphthalene*** (XIII). A portion was crystallised twice from ethanol as white needles, m. p. 190—192° (Found : C, 72·1; H, 6·9. $C_{13}H_{15}O_2N$ requires C, 71·9; H, 6·9%). This enol ether was hydrolysed by warming for 10 min. with 2N-sulphuric acid ; the product separated on cooling. Recrystallisation from water (charcoal) gave 5-acetamido-2-tetralone (2·1 g., 25%) as colourless plates, m. p. 179—180° (Found : C, 70·7; H, 6·4. $C_{12}H_{13}O_2N$ requires C, 70·9; H, 6·4%). The *semicarbazone* crystallised from ethanol in colourless needles, m. p. 233° (Found : C, 60·2; H, 6·4. $C_{13}H_{16}O_2N_4$ requires C, 60·0; H, 6·2%).

5-Acetamido-2-methoxy-1-methylnaphthalene (VIII).—Crude 5-acetamido-1-methyl-2-naphthol (102 g.) in aqueous 2N-sodium hydroxide (1·1 equiv.) was shaken with methyl sulphate (1·05 equiv.) for ½ hr. More sodium hydroxide (2N) and methyl sulphate were then added and shaking continued for a further ½ hr. After a further 2 hr., the excess of methyl sulphate was destroyed by gentle heating on the steam-bath. The crude product (98 g.) was recrystallised from ethanol ; the *methyl ether* (73 g., 68%) separated as large, colourless laths, m. p. 210—211° (Found : C, 73·2; H, 6·7; N, 5·7. $C_{14}H_{15}O_2N$ requires C, 73·5; H, 6·6; N, 6·1%).

6-Methoxy-5-methyl-1-naphthylamine (IX).—5-Acetamido-2-methoxy-1-methylnaphthalene (64 g.) was refluxed for 3 hr. with concentrated hydrochloric acid (400 c.c.), water (100 c.c.), and ethanol (100 c.c.). The solution was then cooled and made alkaline with ammonia. After ½ hr., the precipitated amine was collected, washed with water, and dried (52 g., 99%). This material was suitable for use in the Bucherer reaction ; it had m. p. 124—127°. A portion, recrystallised from benzene (charcoal), gave the *amine* (XI) as colourless needles, m. p. 127—128° (Found : C, 77·1, 77·3; H, 7·1, 7·2; N, 7·1. $C_{12}H_{13}ON$ requires C, 77·0; H, 6·9; N, 7·5%).

6-Methoxy-5-methyl-1-naphthol (X).—A suspension of the foregoing amine (40 g.) in aqueous 40% sodium hydrogen sulphite (1 l.) was stirred vigorously and refluxed for 26 hr. Alternatively the mixture was heated at 100—120° in a rotating autoclave. Aqueous 60% sodium hydroxide (350 c.c.) was then added slowly to the boiling solution with vigorous stirring and the mixture heated until the evolution of ammonia had ceased (*ca.* 4 hr.). After cooling and careful addition of concentrated hydrochloric acid to expel sulphur dioxide the product was allowed to separate overnight. The crude methoxymethylnaphthol (m. p. 137—140° ; 36·9 g., 92%) recrystallised from benzene (charcoal) as colourless needles (27·7 g., 70%), m. p. 143—144° (Part XLV, *loc. cit.*, gives m. p. 142—143°) (Found : C, 76·7; H, 6·4. Calc. for $C_{12}H_{12}O_2$: C, 76·6; H, 6·4%).

The *acetate* prepared by use of acetic anhydride and pyridine crystallised from ethanol in plates, m. p. 145—147° (Found : C, 73·2; H, 6·1. $C_{14}H_{14}O_3$ requires C, 73·1; H, 6·1%).

In our earlier work this naphthol was obtained from the amine (*a*) by diazotisation and

heating of the solution, and also (*b*) by heating with N-sulphuric acid in a sealed tube at 180°. These methods gave unsatisfactory results.

5 : 6 : 7 : 8-*Tetrahydro*-5-*methyl*-6-*oxo*-1-*naphthol* (XI) (cf. Part XLV, *loc. cit.*).—6-Methoxy-5-methyl-1-naphthol (62 g.), suspended in liquid ammonia (800 c.c.) and ethanol (64 c.c.), was reduced by gradual addition, during ½ hr., of sodium (24·7 g.). After evaporation the residue was dissolved in water (500 c.c.), and concentrated hydrochloric acid (200 c.c.) was added. After being shaken for 10 min. the mixture was allowed to cool and the solid was collected. Crystallisation from ethanol (*ca.* 40 c.c.) gave the tetralone (32 g.), m. p. 119—124°, raised to 127—129°, on recrystallisation (27·3 g., 47%) (Part XLV, *loc. cit.*, gave m. p. 127—128°). A small further quantity (0·5 g.) was obtained by stirring the mother-liquors for 30 hr. in ethereal solution with sodium hydrogen sulphite solution and decomposing the aqueous layer with sodium carbonate. The *semicarbazone* separated from ethanol in diamond-shaped, solvated needles, m. p. 170—171° (Found: C, 60·2; H, 7·5. $C_{12}H_{15}O_2N_3,C_2H_6O$ requires C, 60·2; H, 7·5%). The *benzoate* crystallised from ethanol in needles, m. p. 140—141° (Found: C, 77·4; H, 5·5. $C_{18}H_{16}O_3$ requires C, 77·1; H, 5·7%).

5 : 6 : 7 : 9 : 10 : 13-*Hexahydro*-1-*hydroxy*-13-*methyl*-7-*oxophenanthrene* (XVIII).—4-Diethylaminobutan-2-one (21·55 g.) and methyl iodide (9·7 c.c.) were combined by the procedure of Part XLVIII (*loc. cit.*, 1949). 5-Hydroxy-1-methyl-2-tetralone (25 g.) in dry ethanol (150 c.c.) was added with ice-cooling to the methiodide under dry nitrogen, followed by a solution of potassium (16·0 g.) in ethanol (150 c.c.) added in one portion. Swirling was continued for about an hour and until all the methiodide had dissolved. After being kept in ice for a further hour the mixture was boiled gently for ½ hr. and then cooled. 2N-Sulphuric acid (250 c.c.) was added, followed by water (500 c.c.). After 2 hr. the solid was collected and recrystallised from ethanol, to give the phenanthrene derivative (16·9 g., 52%), m. p. 210—212° (Part XLV, *loc. cit.*, 1946, m. p. 208—210°). A portion recrystallised from alcohol had m. p. 212—213° (Found: C, 79·1; H, 6·9. Calc. for $C_{15}H_{16}O_2$: C, 78·9; H, 7·0%). The 2 : 4-dinitrophenylhydrazone separated from acetic acid in red, irregular rhombs, m. p. 244° (decomp.) [Part XLV, *loc. cit.*, m. p. 246° (decomp.)]. The phenol on methylation with methyl sulphate and aqueous alkali gave the known methoxy-ketone (XIX), m. p. 118—120° after crystallisation from light petroleum (b. p. 40—60°) (Part XLV, *loc. cit.*, m. p. 119—120°).

7-*Ethylenedioxy*-5 : 6 : 7 : 8 : 10 : 13-*hexahydro*-1-*methoxy*-13-*methylphenanthrene* (XX; R = Me).—A mixture of the methoxy-ketone (XIX) (20 g.), benzene (400 c.c.), and ethylene glycol (30 c.c.) was slowly distilled with stirring for 1 hr. Toluene-*p*-sulphonic acid (300 mg.) was added and distillation was continued for 4 hr., the volume being maintained by addition of benzene. The cooled solution was washed with saturated sodium hydrogen carbonate solution (100 c.c.) and with water, dried, and evaporated. The residue was triturated with light petroleum (b. p. 40—60°) and crystallised twice from methanol. The *methoxy-ketal* (XX; R = Me) was obtained as colourless prisms (15·7 g.), m. p. 110—111° (Found: C, 75·7; H, 7·8. $C_{16}H_{22}O_3$ requires C, 75·5; H, 7·7%). Concentration of the methanolic mother-liquor and hydrolysis with 2N-hydrochloric acid (20 c.c.) at 100° for 1 hr. allowed 2·4 g. of the ketone to be recovered. The net yield of the ketal was therefore 76%.

From the phenolic ketone (XVIII) (2·3 g.), by a similar procedure, 7-*ethylenedioxy*-5 : 6 : 7 : 8 : 10 : 13-*hexahydro*-1-*hydroxy*-13-*methylphenanthrene* (XX; R = H) (2·2 g., 85%) was obtained, forming pale yellow needles (from ethanol), m. p. 213—214° depressed by starting material (Found: C, 75·0; H, 7·6. $C_{17}H_{20}O_3$ requires C, 75·0; H, 7·4%).

7-*Ethylenedioxy*-5 : 6 : 7 : 8 : 9 : 10 : 13 : 14"β"-*octahydro*-1-*methoxy*-13-*methylphenanthrene* (XXI).—The methoxy-ketal (XX; R = Me) (1 g.) in ethyl acetate (20 c.c.) was shaken with hydrogen at 15°/5 atm. over platinum oxide (120 mg.). After 4 hr. the catalyst and solvent were removed. The residue was triturated with methanol and collected. The methoxy-ketal (XXI) separated from methanol in elongated prisms (600 mg.), m. p. 84—85° (Found: C, 74·8; H, 8·4. $C_{16}H_{24}O_3$ requires C, 75·0; H, 8·3%). The ketal (500 mg.) was boiled for 20 min. with ethanol (5 c.c.) and hydrochloric acid (5 c.c.; 2N). On cooling, the ketone separated; recrystallisation from ethanol gave 5 : 6 : 7 : 8 : 9 : 10 : 13 : 14"β"-octahydro-1-methoxy-13-methyl-7-oxophenanthrene (XXII) in colourless prisms, m. p. 121—122° (350 mg.) (Part XLV, *loc. cit.*, m. p. 120—121°). A specimen of ketone prepared by the earlier method was converted into the ketal by the procedure described above. The product had m. p. 84—85° alone or on admixture with the hydrogenation product (XXI).

5 : 6 : 7 : 8 : 9 : 10 : 13 : 12"α"-*Octahydro*-1-*methoxy*-13-*methyl*-7-*oxophenanthrene* (XXIII).—5 : 6 : 7 : 9 : 10 : 13-Hexahydro-1-methoxy-13-methyl-7-oxophenanthrene (21 g.) in dioxan–ether (1 : 1; 420 c.c.) was slowly added to a stirred solution of lithium (1·9 g.) in liquid ammonia

(1 l.). After 15 min. ammonium chloride (30 g.) was cautiously added and the ammonia was evaporated. Water (500 c.c.) was added and the mixture was extracted twice with chloroform, which was then washed successively with dilute hydrochloric acid, water, aqueous sodium carbonate, and water, dried, and evaporated. The residue on crystallisation from ethanol gave the *trans*-methoxy-ketone (XXIII) in colourless needles, m. p. 156—158° (13·55 g., 65%). A portion recrystallised from ethanol had m. p. 158—159° (Renfrow and Cornforth, *loc. cit.*, gave m. p. 158—159°) (Found: C, 78·6; H, 8·0. Calc. for $C_{16}H_{20}O_2$: C, 78·7; H, 8·2%). The *oxime* crystallised from light petroleum (b. p. 60—80°)–benzene in irregular prisms, m. p. 187—188° (Found: C, 73·8; H, 8·3. $C_{16}H_{21}O_2N$ requires C, 74·1; H, 8·1%). Chromatography of the mother-liquors on alumina gave an additional amount of the above ketone (0·83 g.; m. p. *ca.* 155°, eluted with benzene) and a smaller amount (0·43 g.) of the "β"-alcohol (XXV) (described below), m. p. 115·5—116° (eluted with ether).

5 : 6 : 7 : 8 : 9 : 10 : 13 : 14" α**"-*Octahydro*-7"** β**"-*hydroxy*-1-*methoxy*-13-*methylphenanthrene** (XXV).—**5 : 6 : 7 : 9 : 10 : 13**-Hexahydro-13-methyl-7-oxophenanthrene (1 g.) in ether–dioxan (1 : 1; 40 c.c.) was added slowly with stirring to a mixture of methanol (10 c.c.) and liquid ammonia (250 c.c.). Lithium (400 mg.) was added in small pieces to this solution with stirring during about 15 min. Ammonium chloride (5 g.) was cautiously added and the product was isolated as described in the previous experiment. The product, a brown oil, was dissolved in benzene and chromatographed on acid-washed alumina (*ca.* 30 g.); the portion eluted with ether crystallised on trituration with light petroleum (b. p. 40—60°). The crude product (550 mg.) was recrystallised from this solvent and gave the *methoxy-alcohol* (XXV) as colourless rosettes of needles, m. p. 117·5—118·5° (Found: C, 77·9; H, 8·9. $C_{16}H_{22}O_2$ requires C, 78·1; H, 8·9%). The acetate (acetic anhydride–pyridine) crystallised from light petroleum (b. p. 40—60°) in long, colourless needles, m. p. 107·5—108·5° (Renfrow and Cornforth, *loc. cit.*, gave m. p. 106—107°). The alcohol (XXV) was also obtained when the *trans*-methoxy-ketone (XXIII) (1 g.) was reduced in ether–dioxan with lithium aluminium hydride. After 2 hours' boiling and destruction of excess of hydride with ethyl acetate the product was isolated as usual and crystallised from light petroleum (b. p. 40—60°). Rosettes of colourless needles (800 mg.) were obtained, having m. p. 116—117° alone or mixed with the previous specimen.

5 : 6 : 7 : 8 : 9 : 10 : 13 : 14" α**"-*Octahydro*-1-*hydroxy*-13-*methyl*-7-*oxophenanthrene*** (XXVI).—The phenolic ketone (XVIII) (14 g.) was dissolved in pyridine (50 c.c.) and acetic anhydride (20 c.c.). After 12 hr. at room temperature the mixture was poured into water and the product extracted with benzene. The benzene solution was washed with dilute hydrochloric acid, sodium carbonate solution, and water, then evaporated. The residue was twice evaporated at low pressure with toluene, dissolved in benzene, and poured on acid-washed alumina (*ca.* 110 g.). Elution with benzene and ether–benzene (1 : 4) gave **1-*acetoxy*-5 : 6 : 7 : 9 : 10 : 13-*hexahydro*-13-*methyl*-7-*oxophenanthrene*** (XXIV) (14·9 g., 90%) in colourless irregular rhombs, m. p. 102—104° raised by recrystallisation from aqueous methanol to 104—104·5° (Found: C, 75·3; H, 6·6. $C_{17}H_{18}O_3$ requires C, 75·5; H, 6·7%).

The acetate (15·45 g.) in dioxan–ether (300 c.c.; 1 : 1) was slowly added to a stirred solution of lithium (1·3 g.) in liquid ammonia (1 l.). The blue colour was discharged before the addition was complete and more lithium (*ca.* 0·1 g.) was added in small portions until the blue colour persisted. After a further 15 min. ammonium chloride (30 g.) was added carefully and the ammonia was removed. Water (500 c.c.) was added and the product was extracted with chloroform, which was evaporated after being washed with dilute hydrochloric acid, sodium carbonate solution, and water. The residue on crystallisation from ethanol gave the phenolic trans-*ketone* (XXVI) as a pale yellow crystalline powder (8·57 g., 66%), m. p. 209—211° depressed 2° by the unsaturated ketone (XVIII). From the mother-liquors by acetylation, filtration through alumina, and hydrolysis a further quantity (0·5 g.) of the product was obtained.

The same product (XXVI) was obtained in 33% yield by reduction of the ketone (XVIII) with lithium in ammonia. A sample was obtained in colourless, irregular rhombs, m. p. 209—211°, by shaking in ethanolic solution for 8 hr. with Raney nickel, followed by crystallisation from benzene (Found: C, 78·0; H, 7·8. $C_{17}H_{20}O_3$ requires C, 78·3; H, 7·8%). The acetate crystallised from light petroleum (b. p. 60—80°) and had m. p. 108—110° (Found: C, 75·0; H, 7·3. Calc. for $C_{19}H_{22}O_4$: C, 72·6; H, 7·0%).

A portion of the phenolic ketone (XXVI) on methylation with methyl sulphate and sodium hydroxide gave the methyl ether (XXIII), m. p. and mixed m. p. 158—159° after crystallisation from ethanol.

The saturated and the unsaturated ketone could be conveniently distinguished by colour tests. The material (*ca.* 50 mg.) was dissolved in a mixture of carbon tetrachloride (0·5 c.c.)

and acetic anhydride (0·5 c.c.), and concentrated sulphuric acid (1 drop) was added. On gentle warming the unsaturated ketones (both 1-methoxy and 1-hydroxy) gave deep orange-red colours whereas the saturated ketones gave a transient deep blue colour fading to yellow. Another characteristic test for the unsaturated keto-phenol (XVIII) is the deep red colour developed with aqueous alkali.

7-*Ethylenedioxy*-5 : 6 : 7 : 8 : 9 : 10 : 13 : 14"α"-*octahydro*-1-*methoxy*-13-*methylphenanthrene*.—The *trans*-methoxy-ketone (XXIII) (8·9 g.) was treated with ethylene glycol in the manner described above for the ketone (XIX). The crude product in 1 : 1 benzene–light petroleum (b. p. 40—60°) was filtered through alumina to give the purified *methoxy-ketal* (9·33 g., 95%), m. p. 132—133°; a sample was crystallised from ethanol and obtained in colourless, irregular plates, m. p. 132—133° (Found: C, 75·2; H, 8·6. $C_{18}H_{24}O_3$ requires C, 75·0; H, 8·3%).

7-*Ethylenedioxy*-5 : 6 : 7 : 8 : 9 : 10 : 13 : 14"α"-*octahydro*-1-*methoxy*-13-*methylphenanthrene* (XXVII).—(i) A mixture of the above methoxy-ketal (6·5 g.), potassium hydroxide (13 g.), and methanol (70 c.c.) was heated in an autoclave at 180—190° for 5 hr. When cold, water (200 c.c.) was added and the solution extracted with light petroleum. The aqueous layer was separated and saturated with carbon dioxide. The precipitated phenol was collected by means of ether and passed through a short alumina column in benzene–ether (1 : 1). Recrystallisation of the product from methanol gave the phenolic *ketal* (XXVII) (4·1 g., 65%), m. p. 178—179°. A portion, recrystallised from methanol, formed colourless, irregular prisms, m. p. 179—180° (Found: C, 74·8; H, 8·2. $C_{17}H_{22}O_3$ requires C, 74·4; H, 8·0%). On methylation the methoxy-ketal was regenerated, m. p. and mixed m. p. 132—133° after recrystallisation from methanol. The *acetate* separated from methanol in colourless needles, m. p. 154—155° (Found: C, 71·9; H, 7·6. $C_{19}H_{24}O_4$ requires C, 72·1; H, 7·6%). Inferior yields of the phenol were obtained on raising the autoclave temperature to 210—220°. An attempted demethylation in ethylene glycol at 190° under nitrogen left the starting material unchanged.

(ii) The phenolic *trans*-ketone (XXVI) (7 g.) was treated with ethylene glycol as described above for the ketone (XIX). The crude product, m. p. 170—175°, was passed through alumina in benzene–ether (1 : 1) and crystallised from methanol, to give large colourless prisms (6·6 g., 80%), m. p. 178—179° alone or mixed with the product (XXVII) above.

7-*Ethylenedioxy*-trans-anti-trans-*perhydro*-13-*methyl*-1-*oxophenanthrene* (XXVIII).—The phenolic ketal (XXVII) (5·0 g.) in ethanol (50 c.c.) and aqueous 30% sodium hydroxide (4 drops) was hydrogenated over Raney nickel (W-2; *ca.* 1 g.) at 170°/140 atm. Catalyst and solvent were removed and the residue, dissolved in benzene, was washed four times with 2N-sodium hydroxide and twice with water. After removal of the dried solvent the residue (5·0 g.) was dissolved in pyridine (50 c.c.; purified by treatment with chromic anhydride and subsequent distillation from potassium hydroxide) and added at room temperature to chromium trioxide–pyridine complex [from chromic anhydride (5·0 g.) and pyridine (50 c.c.) according to Sarett *et al.*, *loc. cit.*]. After 12 hr. water (300 c.c.) and benzene–ether (1 : 1; 100 c.c.) were added. The layers were separated after filtration and the aqueous layer was extracted twice more with benzene–ether. The combined extracts were washed twice with water, dried, and evaporated; two distillations at low pressure with toluene then removed traces of pyridine. The crystalline residue was passed through alumina in benzene and recrystallised from methanol, to give the *ketone-ketal* (XXVIII) in clusters of colourless laths, m. p. 113—114·5° (3·7 g., 72%) (Found: C, 73·4; H, 9·2. $C_{17}H_{26}O_3$ requires C, 73·4; H, 9·3%).

trans-anti-trans-*Perhydro*-13-*methyl*-1 : 7-*dioxophenanthrene* (XXIX).—The above ketone-ketal (250 mg.) was boiled gently in acetone (5 c.c.) and 2N-hydrochloric acid (0·1 c.c.) for 20 min. The acetone was removed and water (10 c.c.) added. The crystalline solid was collected and recrystallised from light petroleum (b. p. 60—80°), to give the diketone (XXIX) as thin plates, m. p. 81—82° (Renfrow and Cornforth, *loc. cit.*, gave m. p. 79—81°) (Found: C, 76·7; H, 9·3. Calc. for $C_{15}H_{22}O_2$: C, 76·9; H, 9·4%). The ketone tends to separate in a hydrated form and comparison with an authentic specimen was easier after recrystallisation of each sample from *cyclo*hexane without precautions to exclude water. The m. p. and mixed m. p. of both samples were then 72—74° and the infrared spectra (in potassium bromide; kindly determined by Dr. R. K. Callow) were identical. As a further check the ketone-ketal (XXIX) was converted in the usual manner into the di(ethylene ketal), which crystallised from light petroleum (b. p. 60—80°) in small needles, m. p. 150—152° (Renfrow and Cornforth, *loc. cit.*, gave m. p. 149—150°) (Found: C, 70·8; H, 9·1. Calc. for $C_{19}H_{30}O_4$: C, 70·8; H, 9·3%).

Reaction of the Ketone-ketal (XXVIII) *with Methyl Oxalate*.—Sodium (166 mg.) was dissolved in methanol (2 c.c.), and the solution evaporated at 120° *in vacuo*. The cake of sodium methoxide was broken up, nitrogen was passed in, and methyl oxalate (0·85 g.) and benzene (4 c.c.)

were added. The mixture was refluxed for 10 min., after which a solution of the ketone-ketal (XXVIII) (1 g.) in benzene (6 c.c.) was added. After 4 hr. at room temperature, water (15 c.c.) was added and the benzene layer was separated and extracted twice with 2N-sodium hydroxide. The combined aqueous extracts were saturated with carbon dioxide and extracted with chloroform, which was then washed with water, dried, and evaporated. The residue, after being digested with a little methanol, was collected [300 mg.; m. p. 208—210° (decomp.)]. Crystallisation from methanol gave **7-*ethylenedioxy*-2 : 3 : 4 : 5 : 6 : 7 : 8 : 9 : 10 : 12'' α '' : 13 : 14'' α ''-*dodecahydro*-1-*hydroxy*-13-*methyl*-2-*phenanthrylideneglycollic lactone*** (XXX) in irregular rhombs, m. p. 220—222° (decomp.) (Found : C, 68·8; H, 7·0. $C_{19}H_{24}O_5$ requires C, 68·7; H, 7·2%). The lactone gave no colour with alcoholic ferric chloride and was soluble in cold aqueous alkali. The infrared absorption spectrum (in Nujol) showed a carbonyl band at 5·75 and a hydroxyl band at 2·8 μ. The ultraviolet absorption (in $CHCl_3$) showed a sharp maximum at 2950 Å (ε 29,500).

The lactone (100 mg.) in ether containing a drop of methanol was methylated with diazomethane (from 1 g. of methylnitrosourea). Removal of the solvent and crystallisation from methanol gave the lactonic ***α-methyl ether*** in needles, m. p. 170—172° (Found : C, 68·9; H, 7·5. $C_{20}H_{26}O_5$ requires C, 69·3; H, 7·5%). The infrared absorption spectrum (in Nujol) had a carbonyl band at 5·73 μ but no hydroxyl band. Ultraviolet absorption : $\lambda_{max.}$ 2975 Å (ε 22,200 in $CHCl_3$).

Methyl 7-*Ethylenedioxy*-trans-anti-trans-*perhydro*-13-*methyl*-1-*oxophenanthrene*-2-*carboxylate* (XXXI).—The ketone-ketal (XXVIII) (1 g.), methyl carbonate (6·5 c.c.), and methanol (2 drops) were added to a suspension of sodium hydride (0·21 g.) in dry ether (8 c.c.). The mixture was stirred rapidly for 16 hr. with five ¼" ball-bearings and 2 g. of powdered glass. A mixture of water (10 c.c.) and ether (10 c.c.) was then added with rapid stirring and the whole filtered. The residue was suspended in saturated aqueous sodium dihydrogen phosphate and extracted with chloroform; the ethereal filtrate was washed with sodium dihydrogen phosphate solution. The chloroform and ether solutions were washed with water and evaporated and the residues combined. Crystallisation from methanol gave, in two crops, the *keto-ester* (XXXI) as small needles (700 mg., 65%), m. p. 120—124° raised by further crystallisation to 124—126° (Found : C, 67·5; H, 8·1. $C_{19}H_{28}O_5$ requires C, 67·8; H, 8·3%). The keto-ester gave a blue colour with alcoholic ferric chloride.

Methyl 7-*Ethylenedioxy*-trans-anti-trans-*perhydro*-2''ξ'':13-*dimethyl*-1-*oxophenanthrene*-2''ξ''-*carboxylate* (XXXII).—The keto-ester (XXXI) (2·2 g.) in dry benzene (18 c.c.) was added to sodium (1·43 g.) in methanol (33 c.c.). The mixture was refluxed with stirring for ½ hr., the sodio-derivative separating. After cooling, methyl iodide (4·5 c.c.) was added and the mixture was stirred at room temperature. After 45 min. more methyl iodide (45 c.c.) was added and after a further 30 min. the reaction was completed by refluxing the clear yellow solution for 45 min. Saturated sodium dihydrogen phosphate solution was added, the organic layer was separated, and the aqueous layer was extracted twice with ether. The combined extracts were washed with 2N-sodium hydroxide and with water, dried, and evaporated. The residue (2·22 g.) was crystallised from a little ether, the methylated *keto-ester* (XXXII) being obtained as irregular prisms, m. p. 140—142° (1·45 g.) raised by further crystallisation to 141—142·5° (Found : C, 68·7; H, 8·4. $C_{20}H_{30}O_5$ requires C, 68·6; H, 8·6%). The substance gave no colour with alcoholic ferric chloride. The mother-liquor, possibly containing an epimer, was carefully chromatographed on alumina but the only crystalline material isolated was more of the above isomeride (150 mg.), making the total yield 70%.

Methyl trans-anti-trans-*Perhydro*-2''ξ'':13-*dimethyl*-1:7-*dioxophenanthrene*-2''ξ''-*carboxylate* (XXXIII).—The above keto-ester (XXXII) (150 mg.) in acetone (5 c.c.) and 2N-hydrochloric acid (0·05 c.c.) was refluxed for 15 min. The acetone was removed and water (10 c.c.) was added. The resulting solid was collected, washed with water, and dried (120 mg.; m. p. 125—127°). Crystallisation from light petroleum gave the *diketo-ester* as rhombs, m. p. 127—129° (Found : C, 70·7; H, 8·6. $C_{18}H_{26}O_4$ requires C, 70·6; H, 8·5%).

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Methoxylated Hexahydro-9 : 11-dimethylcarbazoles.

By M. F. Millson and Sir Robert Robinson.

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The hexahydro-*Bz*-methoxycarbazoles were found to be unsuitable as models for the colour reactions of indole alkaloids, doubtless because of oxidative changes. To avoid the latter the 3-position of the indole nucleus was fully substituted and the four hexahydro-*Bz*-methoxy-9 : 11-dimethylcarbazoles were prepared; their colour reactions and ultraviolet absorption spectra are described.

This investigation arose from a desire to facilitate comparisons of characteristic properties of certain indole alkaloids with model substances such that the position of a methoxyl group in the benzene nucleus could be virtually determined.

When we started the work it was thought that akuammine (Henry and Sharp, *J.*, 1927, 1950; Henry, *J.*, 1932, 2759) was a hydro-*Bz*-methoxyindole derivative, but it was later recognised as a phenol (Millson, Robinson, and Thomas, *Experientia*, 1953, **9**, 89). Nevertheless the oxidative reactions in acid solution and the ultraviolet absorption spectrum are quite close to those of bases derived from *p*-anisidine or *p*-phenetidine. Some notes on the chemistry of akuammine will, it is hoped, be submitted to the Society in a short time but the following Table and the light absorption data (see Fig. 1) suffice to make a good *prima facie* case for the *p*-aminophenol orientation. This is confirmed in the sequel.

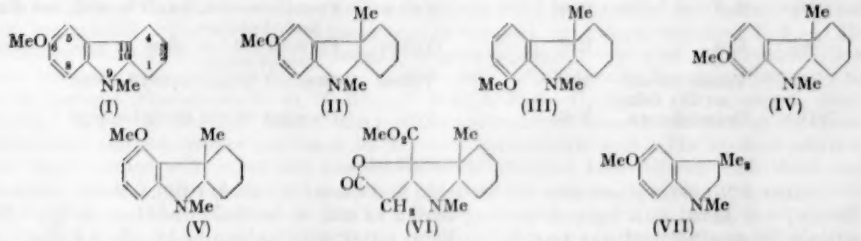
Substance	$FeCl_3$ in dil. HCl	$NaNO_2$ in acid soln. : original	on basification	Action of diazobenzenesulphonic acid
Akuammine ...	Orange-brown	Yellow-orange	Red	Does not form a methyl-orange
Strychnidine	Red	Red	Yellow	Forms a methyl-orange
Brucidine	Olive-green	Yellow-orange	Red	Does not form a methyl-orange
α-Colubridine (*m*-anisidine)	Red	Orange	Little change	Faint reaction
β-Colubridine (*p*-anisidine)	Orange	Yellow-orange	Darkens	Faint reaction
Eserethole	Orange-brown	Yellow	Red	No reaction
Hexahydro-9-methylcarbazole	Red	Red	Yellow	Forms a methyl-orange

One of the first substances we examined was 1 : 2 : 3 : 4 : 10 : 11-hexahydro-6-methoxy-9-methylcarbazole (I) which was prepared by standard methods. This substance resembled akuammine in its ultraviolet absorption spectrum and its failure to couple with diazobenzenesulphonic acid but under the influence of oxidising agents, even ferric chloride, a copious flocculent precipitate of the tetrahydrocarbazole was obtained. For this reason we turned to similar substances bearing a methyl group in position 11, as in (II). This substance was synthesised by two recognised methods, and then starting from *o*-anisidine we prepared (III).

From *m*-anisidine, two isomerides, one liquid and one crystalline, were obtained and separated by chromatography and distillation. The liquid isomer is 1 : 2 : 3 : 4 : 10 : 11-hexahydro-7-methoxy-9 : 11-dimethylcarbazole (IV), and the solid is the 5-methoxy-isomeride (V).

This conclusion follows from a study of the infrared absorption of the compounds (II)—(V) in the region 12—14 μ. The carbazoles (II) and (IV) are thus seen to be 1 : 2 : 4-unsubstituted [*i.e.*, unsubstituted at positions 5, 7, and 8 of (I)], whereas the isomers (III) and (V) contain three vicinal unsubstituted hydrogen atoms. In addition the phenol related to (IV) gives a rhodamine of normal type, whereas that derived from the solid isomer (V) gives a brilliant rhodamine exhibiting a quite different colour and fluorescence. A normal rhodamine is also obtained from α-colubridine, the benzene nucleus of which is known to be substituted as in (IV) (Warnat, *Helv. Chim. Acta*, 1931, **14**, 997). This was established by degradation to the related methoxyoxanthranilic acid. The yield was unfavourable, and in a similar permanganate oxidation of brucine, Späth and Bretschneider

(*Ber.*, 1930, **63**, 2997) obtained 4 : 5-dimethoxyoxanthranilic acid in a yield of only 0·23% of the theoretical. An attempt to distinguish between the isomers (IV) and (V) in this way was not made because it was found that the 6-methoxy-compound (II) was changed



by potassium permanganate into a product which was esterified by diazomethane and was then found to be neutral and to give analyses corresponding to the formula $C_{14}H_{21}O_4N$.

Absorption Spectra.

FIG. 1.

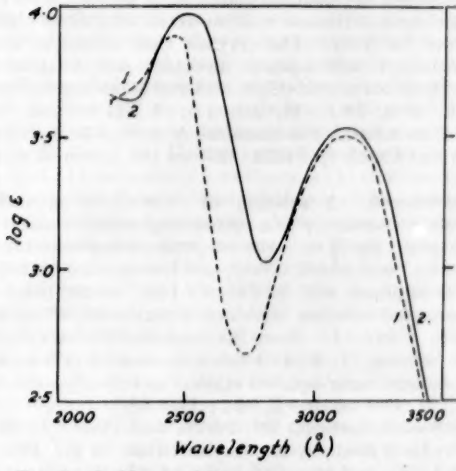


FIG. 2.

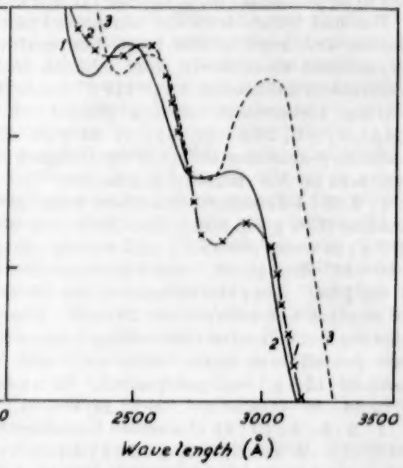


FIG. 1. 1, Akuammine.
2, 1 : 2 : 3 : 4 : 10 : 11-Hexahydro-6-methoxy-9 : 11-dimethylcarbazole (II).

FIG. 2. 1, 1 : 2 : 3 : 4 : 10 : 11-Hexahydro-8-methoxy-9 : 11-dimethylcarbazole (III).
2, 1 : 2 : 3 : 4 : 10 : 11-Hexahydro-5-methoxy-9 : 11-dimethylcarbazole (solid) (V)
3, 1 : 2 : 3 : 4 : 10 : 11-Hexahydro-7-methoxy-9 : 11-dimethylcarbazole (liquid) (IV).

It is possible to suggest several structures [of which (VI) is an example] for this substance but they are all based on the assumption that the benzene nucleus has been broken up. As our objective had been reached in another way it seemed unnecessary to carry the matter further. 5-Methoxy-1 : 3 : 3-trimethylindoline (VII) and some hexahydro-9-methylcarbazoles have been prepared for additional comparisons.

The following Table gives some of the colour reactions of the methoxylated bases and Figs. 1 and 2 show the ultraviolet absorptions.

In addition, only compounds (IV) and (V) give rise to rhodamines, and the isomer (II) gives an intense, stable, red-purple colour on the addition of a little dichromate to a solution in dilute sulphuric acid.

Dr. H. T. Openshaw has very kindly sent us details of quite similar results which he and Mr. J. R. Chalmers have obtained with the isomeric hexahydromethoxycarbazoles, studied in connexion with the constitution of aspidospermine.

Substance	$FeCl_3$ in dil. HCl	$NaNO_2$ in acid soln. : original	on basification	Action of diazobenzenesulphonic acid
(II)	Orange-brown	Yellow (dil. soln.)	Red	Does not form a methyl-orange
(III)	Magenta	Red	Yellow	Forms a methyl-orange
(IV)	Red	Red	Yellow	Forms a reddish colour in acid, but not a methyl-orange
(V)	Red	Red	Yellow	Forms a reddish colour in acid, but not a methyl-orange
(I)	Yellow-brown, rapidly fading	Yellow	Yellow	Does not form a methyl-orange
(VII)	Orange-brown	Yellow	Red	Does not form a methyl-orange

Experimental

N-Methyl-N-nitroso-p-anisidine (cf. Hodgson and Crook, *J.*, 1932, 1812).—Methyl sulphate (30 c.c.) was added with vigorous swirling during 15 min. to molten *p*-anisidine (50 g.). The mixture became hot and was kept for an hour, mixed with sodium hydroxide solution, and steam-distilled. The isolated, mixed bases were dissolved in hydrochloric acid (150 c.c.; *d* 1·16) and water (100 c.c.). Sodium nitrite (40 g.) in water (200 c.c.) was added to the stirred solution initially at 0° and always below 5°. The pale brown precipitate of *N*-methyl-*N*-nitroso-*p*-anisidine was collected, washed with water, and dried (20·5 g.); after crystallisation from light petroleum (b. p. 60—80°) it was obtained as colourless plates, m. p. 46—47° (15·9 g.).

The acid filtrate from the nitrosation mixture was treated with an excess of sodium nitrite solution and kept at the room temperature for 1 hr. The crystals that separated were recrystallised successively from ethanol, methanol, and aqueous methanol and obtained as almost colourless needles, m. p. 111·5°, insoluble in hot or cold dilute acid and alkali and showing a strong Liebermann reaction (Found : C, 37·8, 37·4; H, 3·7, 3·2; N, 21·8. Calc. for $C_8H_8O_6N_4$: C, 37·5; H, 3·1; N, 21·9%). The substance is therefore *N*-methyl-3 : 5-dinitro-*N*-nitroso-*p*-anisidine obtained by Hodgson and Crook (*J.*, 1933, 825) by the action of dilute nitric acid on *NN*-dimethyl-*p*-anisidine.

1 : 2 : 3 : 4-*Tetrahydro-6-methoxy-9-methylcarbazole*.—A solution of *N*-methyl-*N*-nitroso-*p*-anisidine (15·9 g.) in acetic acid (26·5 c.c.) was added slowly to a stirred suspension of zinc dust (26·5 g.) in water (40·5 c.c.), and stirring continued for 1½ hr.; the temperature was maintained at 10—15° throughout. *cycl*Hexanone (9·8 c.c.) was added slowly, and the mixture heated to 80° for ½ hr. After the addition of hot dilute sulphuric acid (23 c.c. of *d* 1·84; water, 104 c.c.), the mixture was refluxed for 20 min. The cooled solution deposited a pink solid which was collected and extracted with boiling ethanol (4 × 40 c.c.). When the combined filtered extracts were poured into water (1500 c.c.) with stirring, 1 : 2 : 3 : 4-*tetrahydro-6-methoxy-9-methylcarbazole* (13·5 g.) was precipitated. It crystallised from aqueous ethanol as colourless needles, m. p. 88—89° (Found : C, 78·2; H, 9·0. $C_{14}H_{17}ON$ requires C, 78·1; H, 8·0%).

1 : 2 : 3 : 4 : 10 : 11-*Hexahydro-6-methoxy-9-methylcarbazole* (cf. Perkin and Plant, *J.*, 1924, 1512) (I).—A mixture of 1 : 2 : 3 : 4-tetrahydro-6-methoxy-9-methylcarbazole (5 g.), ethanol (8·6 c.c.), concentrated hydrochloric acid (8·6 c.c.), and granulated tin (8·6 g.) was refluxed for 3 hr. The hot solution was filtered, and the residue washed with a hot mixture of ethanol (3 c.c.) and concentrated hydrochloric acid (3 c.c.). The combined filtrates were cooled, made alkaline, and steam-distilled. The distillate was basified with ammonia and extracted with ether. The dark residual oil from the dried extract afforded 1 : 2 : 3 : 4 : 10 : 11-*hexahydro-6-methoxy-9-methylcarbazole* (3·2 g.) as a colourless oil, b. p. 188—189°/21 mm., which rapidly darkened in the air (Found : C, 77·6; H, 8·8; N, 6·5. $C_{14}H_{19}ON$ requires C, 77·4; H, 8·8; N, 6·5%); the *picrate* formed yellow plates (from ethanol), m. p. 132·5—133° (Found : C, 53·6; H, 4·8; N, 12·3. $C_{14}H_{19}ON,C_6H_3O_7N_3$ requires C, 53·8; H, 5·0; N, 12·6%).

2 : 3 : 4 : 11-*Tetrahydro-6-methoxy-9* : 11-*dimethylcarbazole and* 1 : 2 : 3 : 4-*Tetrahydro-6-methoxy-1* : 9-*dimethylcarbazole*.—(i) *N*-Methyl-*N*-nitroso-*p*-anisidine (11·4 g.) was reduced as above with zinc dust (18·9 g.) in acetic acid (18·9 c.c.) and water (28·7 c.c.). 2-Methyl*cyclo*hexanone (8 c.c.) was introduced and the mixture kept at 80° for 30 min. Hot dilute sulphuric acid (16·4 c.c. of *d* 1·84; water, 74 c.c.) was then added and the mixture was refluxed for 20 min. The cooled solution was extracted several times with ether (A). The aqueous layer was mixed with saturated picric acid solution, and the *N*-methyl-*p*-anisidine picrate which separated was collected and crystallised from ethanol, forming yellow rods, m. p. 159° (Found : C, 46·3; H, 3·8; N, 15·1. Calc. for $C_8H_{11}ON,C_6H_3O_7N_3$: C, 45·9; H, 3·9; N, 15·3%).

On evaporation of the dried ethereal extract (A) 1 : 2 : 3 : 4-*tetrahydro-6-methoxy*-1 : 9-*dimethylcarbazole* was obtained as a colourless solid which crystallised from ethanol in needles

(1·9 g.), m. p. 75—76°, rapidly reddening in air (Found : C, 78·4; H, 8·4. $C_{15}H_{19}ON$ requires C, 78·6; H, 8·4%).

(ii) (cf. Plancher *et al.*, *Gazzetta*, 1929, **59**, 334). A mixture of **1 : 2 : 3 : 4-tetrahydro-6-methoxy-9-methylcarbazole** (10·9 g.) and methyl iodide (55 g.) was heated in a sealed tube at 116° for 10 hr. The light brown crystalline mass was freed from methyl iodide and extracted with hot ethanol. The solution, on being kept in the dark for 3 days, deposited ***2 : 3 : 4 : 11-tetrahydro-6-methoxy-9 : 11-dimethylcarbazole hydriodide*** as pale brown needles. Recrystallisation from ethanol gave colourless prisms, m. p. 186—187°, which became brown on exposure to air or daylight (Found : C, 50·4; H, 5·8; N, 3·8; I, 35·3. $C_{15}H_{19}ON,HI$ requires C, 50·4; H, 5·6; N, 3·9; I, 35·5%). Most of the ethanol was removed from the solution of the crude hydriodide, and the residue was taken up in dilute hydrochloric acid. The aqueous solution was twice washed with ether and basified, and the liberated base isolated with ether and distilled. **2 : 3 : 4 : 11-*Tetrahydro-6-methoxy*-9 : 11-*dimethylcarbazole*** was obtained as a pale yellow oil, b. p. 146—147°/0·5 mm. (Found : C, 79·0; H, 8·6; N, 6·0. $C_{15}H_{19}ON$ requires C, 78·6; H, 8·4; N, 6·1%). The picrate forms rosettes of fine, yellow needles, m. p. 140·5°, from ethanol (Found : C, 54·8; H, 4·5; N, 11·9. $C_{15}H_{19}ON,C_6H_3O_7N_3$ requires C, 55·0; H, 4·8; N, 12·2%).

(iii) *N*-Methyl-*N*-nitroso-*p*-anisidine (43·6 g.) was reduced with zinc dust and acetic acid as described above. The *N*-*p*-methoxyphenyl-*N*-methylhydrazine was isolated and distilled (20·5 g.). It was heated on the steam-bath with 2-methyl*cyclo*hexanone (15 c.c.), finally ***in vacuo*** until all the water was removed. After addition of acetic acid (250 c.c.) the mixture was refluxed for 30 min. Most of the acetic acid (190 c.c.) was removed under reduced pressure, and water (200 c.c.) and concentrated hydrochloric acid (20 c.c.) were added to the residue, after which the whole was several times washed with ether. The aqueous solution was made alkaline and the liberated bases were isolated with ether and distilled. The colourless oil, b. p. 60—115°/0·01 mm., was not further purified, but was immediately hydrogenated (see below).

1 : 2 : 3 : 4 : 10 : 11-*Hexahydro-6-methoxy*-9 : 11-*dimethylcarbazole* (II).—(*A*) A solution of **2 : 3 : 4 : 11-tetrahydro-6-methoxy-9 : 11-dimethylcarbazole** (3·1 g.) (see ii, above) in ethanol (50 c.c.) was shaken under hydrogen at the room temperature and pressure in the presence of 10% palladised charcoal. Absorption of hydrogen ceased after 100 min., when 300 c.c. of hydrogen had been taken up (theor. for $1H_2$, 315 c.c.). The solution was filtered, concentrated, and distilled; **1 : 2 : 3 : 4 : 10 : 11-*hexahydro-6-methoxy*-9 : 11-*dimethylcarbazole*** (2·9 g.) was collected at 148°/0·5 mm. as a colourless oil. This solidified, and crystallisation from a very small volume of light petroleum (b. p. 40—60°) gave colourless needles, m. p. 43—44° (Found : C, 78·1; H, 9·4; N, 5·9; *C*-Me, 3·7. $C_{15}H_{21}ON$ requires C, 77·9; H, 9·1; N, 6·1; *C*-Me, 6·5%). The base forms a *picrate*, pale yellow plates from ethanol (Found : C, 55·1; H, 5·1; N, 12·1. $C_{15}H_{21}ON,C_6H_3O_7N_3$ requires C, 54·8; H, 5·3; N, 12·2%), the m. p. (decomp.) of which varies over the range 155—169° according to the rate of heating; in a bath preheated to 155°, rapid heating results in decomposition at 169°.

(*B*) The colourless oil, b. p. 60—115°/0·01 mm. (see iii above), dissolved in ethanol (100 c.c.), was shaken under hydrogen with 10% palladised charcoal at the room temperature and pressure. No absorption of hydrogen occurred under these conditions, or at 50°. The solution was filtered and hydrogenation repeated using Raney nickel at 45°; 900 c.c. of hydrogen were absorbed in 12 hr. The filtered solution was concentrated, and the residual oil fractionated, giving : (*a*) *N*-methyl-*p*-anisidine, b. p. 48—57°/0·003 mm., m. p. 38°; (*b*) b. p. 88—90°/0·003 mm., a colourless oil which was again fractionated; then the oil, b. p. 85—88°/0·01 mm., solidified and had m. p. 42—43°. After crystallisation from light petroleum (b. p. 40—60°), it was obtained as colourless needles, m. p. 44—45°, identical with that obtained by the procedure (*A*) as shown by undepressed mixed m. p. and by the similar behaviour of the picrates.

1 : 2 : 3 : 4-*Tetrahydro-8-methoxy-9-methylcarbazole*.—*o*-Anisidine (100 g.) was methylated with methyl sulphate as described for *p*-anisidine. The mixture of bases obtained was dissolved in dilute sulphuric acid (65 c.c. of *d* 1·84; water, 1000 c.c.) and, while the solution was vigorously stirred with ether (200 c.c.), sodium nitrite (42 g.) in water (200 c.c.) was added at <5°. The ethereal layer was separated, and the aqueous solution extracted with ether. Removal of the solvent from the combined, dried, ethereal solutions left the nitrosamine as a dark oil (44 g.).

The crude nitrosamine was reduced as was *N*-nitroso-*p*-anisidine (above), with zinc dust and acetic acid. *cyclo*Hexanone (27 c.c.) was added to the stirred suspension, and the mixture was heated at 80° during 1 hr. and then refluxed with dilute sulphuric acid (88 c.c. of *d* 1·84; water, 420 c.c.) for 20 min. The acidic suspension, containing a red oil, was extracted with ether,

and the extract was washed with dilute sodium hydroxide solution and water, and dried ($MgSO_4$). After evaporation of the ether, most of the *cyclo*hexanone was removed *in vacuo*. The residue partly crystallised overnight, and the crystals were collected; by further concentration of the mother-liquors a second crop was obtained. Recrystallisation of the combined crops from ethanol furnished pure **1 : 2 : 3 : 4-*tetrahydro*-8-*methoxy*-9-*methylcarbazole*** (4·0 g.), colourless needles, m. p. 100—101° (Found: C, 78·4; H, 8·2; N, 6·8. $C_{14}H_{17}ON$ requires C, 78·1; H, 8·0; N, 6·5%).

In a later preparation the reaction mixture from the reduction of the nitrosamine and treatment with *cyclo*hexanone was heated on the steam-bath for 2 hr., cooled, and extracted with ether. The ether was removed from the undried extract, and the resultant black oil (*e.g.*, 20 g.) was added to acetic acid (50 c.c.), concentrated sulphuric acid (2 c.c.), and water (160 c.c.), and the whole was refluxed for 35—45 min. The cooled suspension was extracted with ether, and the extract freed from acetic acid with dilute sodium hydroxide solution and washed with water. The residue from the dried extract was distilled, giving **1 : 2 : 3 : 4**-tetrahydro-8-methoxy-9-methylcarbazole, b. p. 180—210°/15 mm. Attempts to methylate this base with methyl iodide were unsuccessful.

2 : 3 : 4 : 11-*Tetrahydro*-8-*methoxy*-9 : 11-*dimethylcarbazole*.—Crude *N*-methyl-*N*-nitroso-*o*-anisidine (48·5 g.) was reduced in the usual manner. The product was heated with 2-methyl-*cyclo*hexanone (34 c.c.) on the steam-bath for 2 hr., cooled, and extracted with ether. The oily residue (66 g.) from the dried extract was divided into three equal portions. One portion was refluxed with a mixture of acetic acid and dilute sulphuric acid, another with acetic acid (above). Extraction of the diluted and basified solutions with ether afforded small quantities of yellow oils, b. p. 200—210°/2 mm. and 140—160°/1 mm., respectively.

The third portion of the crude hydrazone was heated at 60—80° with 10% sulphuric acid (200 c.c.) for 11 hr. After being washed with ether the solution was basified and again extracted and the product distilled. Recovered *N*-methyl-*o*-anisidine, b. p. 103—105°/10 mm., m. p. 31—33°, was followed by an almost colourless oil, b. p. 140—170°/2 mm., which solidified on keeping at −5° in about 3 weeks (m. p. 45—61°).

The small higher-boiling fractions from the first two portions of crude hydrazone were cooled to −5° and seeded with this solid; they partly crystallised, but were liquid at the room temperature. This product (1·2 g.) was triturated with a small volume of light petroleum (b. p. 40—60°), cooled in carbon dioxide–ethanol. The crystals so obtained were combined with the material, m. p. 45—61°, and recrystallised from light petroleum (b. p. 40—60°), to give **2 : 3 : 4 : 11-*tetrahydro*-8-*methoxy*-9 : 11-*dimethylcarbazole*** (*ca.* 250 mg.) as colourless needles, m. p. 79—80° (Found: C, 78·6; H, 8·1; N, 6·3. $C_{15}H_{19}ON$ requires C, 78·6; H, 8·4; N, 6·1%). The *picrate*, yellow rods from ethanol, had m. p. 215° (decomp.) (Found: C, 55·1; H, 4·7. $C_{15}H_{19}ON,C_6H_3O_7N_3$ requires C, 55·0; H, 4·8%). A specimen of this picrate was oxidised by air during recrystallisations from ethanol, giving a *picrate* which formed green rods, m. p. 210—212° (Found: C, 53·6; H, 4·3; N, 11·9. $C_{15}H_{17}O_2N,C_6H_3O_7N_3$ requires C, 53·4; H, 4·3; N, 11·9%).

1 : 2 : 3 : 4 : 10 : 11-*Hexahydro*-8-*methoxy*-9 : 11-*dimethylcarbazole* (III).—Crude *N*-methyl-*N*-nitroso-*o*-anisidine (46 g.) was reduced and the product treated with 2-methyl*cyclo*hexanone (30 c.c.) as described above. The dark oil (75 g.) was heated at 80° with 10% sulphuric acid (500 c.c.) for 11 hr. and worked up as already described. The product, b. p. 140—145°/1 mm., was a thick yellow oil (1·75 g.) which largely solidified when seeded with **2 : 3 : 4 : 11**-tetrahydro-8-methoxy-9 : 11-dimethylcarbazole. It was dissolved in ethanol (40 c.c.) and shaken under hydrogen with Raney nickel at 60°. After 12 hr., about 150 c.c. of hydrogen had been absorbed. The filtered solution was distilled and **1 : 2 : 3 : 4 : 10 : 11-*hexahydro*-8-*methoxy*-9 : 11-*dimethylcarbazole*** (1 g.) was obtained as a colourless viscous oil, b. p. 103—105°/0·06 mm. (Found: C, 78·1; H, 9·2. $C_{15}H_{21}ON$ requires C, 77·9; H, 9·1%).

m-*Anisidine*.—A solution of *m*-nitroanisole (160 g.) (cf. *Org. Synth.*, Coll. Vol. I, 2nd edn., p. 404; Hodgson and Nixon, *J.*, 1930, 2166) in ethanol (400 c.c.) was shaken with Raney nickel under hydrogen at 95°/90 atm.; after removal of the solvent the base was purified by dissolution in dilute hydrochloric acid, washing with ether, basification, isolation with ether, and distillation. *m*-Anisidine (121 g.) was obtained as a colourless oil, b. p. 123—125°/15 mm.

N-*Methyl*-m-*anisidine*.—(*a*) An attempted methylation of *m*-anisidine with methyl iodide in ether resulted in the separation of *m*-anisidine hydriodide which crystallised from methanol–ether in colourless needles, m. p. 175—177° (Found: C, 33·9; H, 4·0. Calc. for C_7H_9ON,HI: C, 33·5; H, 4·0%).

(*b*) Methyl sulphate (49·2 c.c.) was added dropwise and with swirling to *m*-anisidine (82 g.)

initially at 60°. The hot products were cooled, poured into an excess of sodium hydroxide solution, and steam-distilled. The bases were isolated from the distillate with ether, and distilled; crude *N*-methyl-*m*-anisidine (80 g.) was obtained as a pale yellow oil, b. p. 118—119·5°/8 mm.

(*c*) Benzene (300 c.c.) was added to an intimate mixture of powdered sodamide (17·6 g.) and powdered *N*-acetyl-*m*-anisidine (71 g.). When the evolution of ammonia slackened, the mixture was refluxed until it suddenly became a gel. The benzene was then removed under diminished pressure and ether (300 c.c.) added to the hard white residue. Methyl iodide (61 g.) was added and the mixture kept for 2 hr. and then refluxed for 11 hr. After addition of water (400 c.c.) the ethereal layer was washed with dilute acid and water, and evaporated, giving N-*acetyl*-N-*methyl*-m-*anisidine* as a colourless solid; crystallisation from light petroleum (b. p. 40—60°) gave colourless prisms (48 g.), m. p. 64° (Found : C, 67·0; H, 7·4; N, 7·5. $C_{10}H_{13}O_2N$ requires C, 67·0; H, 7·3; N, 7·8%). This derivative (19·6 g.) was refluxed with 25% sulphuric acid (400 c.c.) for 2 hr. The cooled solution was basified, and the base isolated with ether and distilled. N-*Methyl*-m-*anisidine* (13·8 g.) was obtained as a colourless oil, b. p. 131°/17 mm. (Found : C, 70·2; H, 8·2; N, 10·3. $C_8H_{11}ON$ requires C, 70·0; H, 8·1; N, 10·2%). The picrate formed yellow or red-brown prisms (from ethanol), m. p. 147° (decomp.) (Found : C, 46·0, 46·2; H, 3·9, 3·7; N, 15·6, 15·1. $C_8H_{11}ON,C_6H_3O_7N_3$ requires C, 45·9; H, 3·9; N, 15·3%).

N-*Methyl*-N-*nitroso*-m-*anisidine*.—A solution of *N*-methyl-*m*-anisidine (15 g.) in 6% hydrochloric acid (65 c.c.) was vigorously agitated with ether (50 c.c.) at 5—10° during the addition of a solution of sodium nitrite (8 g.) in water (20 c.c.) until the aqueous layer gave an immediate colour with starch–cadmium iodide paper. The ethereal layer was separated, washed with sodium hydrogen carbonate solution, and with water, and dried. On evaporation of the ether, the crude *nitrosamine* remained as a golden-yellow oil; a portion was distilled as a yellow oil, b. p. 98°/0·1 mm. (Found : C, 57·6; H, 6·4; N, 16·9. $C_8H_{10}O_2N_2$ requires C, 57·8; H, 6·1; N, 16·9%).

2-*Methyl*cyclo*hexanone* N-m-*Methoxyphenyl*-N-*methylhydrazone and* 2 : 3 : 4 : 11-*Tetrahydro*-5- *and* -7-*methoxy*-9 : 11-*dimethylcarbazole*.—Crude *N*-methyl-*N*-nitroso-*m*-anisidine (14 g.) was reduced to *N*-*m*-methoxyphenyl-*N*-methylhydrazine (8 g. crude, distilled) by the method of Kermack, Perkin, and Robinson (*J.*, 1922, **121**, 1872). The crude hydrazine was heated on the steam-bath with 2-methyl*cyclo*hexanone (9 c.c.), first at atmospheric pressure for ½ hr., and then under reduced pressure until no more water was evolved. A portion of the *hydrazone* was distilled, and again was a colourless liquid, b. p. 90—95°/0·005 mm., rapidly darkening in air (Found : C, 73·0; H, 9·1; N, 11·4. $C_{15}H_{22}ON_2$ requires C, 73·1; H, 9·0; N, 11·4%).

The remainder of the crude hydrazone was refluxed with acetic acid (100 c.c.) for 30 min., and the mixture then evaporated under reduced pressure. The residue was taken up in dilute hydrochloric acid, the solution was washed with ether and basified with ammonia, and the liberated bases were isolated with ether and distilled. The fraction of b. p. 95—110°/0·005 mm. was redistilled, yielding a mixture of 2 : 3 : 4 : 11-tetrahydro-5- and -7-methoxy-9 : 11-dimethylcarbazole as a colourless liquid, b. p. 94—95° (bath)/0·001 mm., rapidly becoming yellow in air (Found : C, 78·3; H, 8·8; N, 6·2. Calc. for $C_{15}H_{19}ON$: C, 78·6; H, 8·4; N, 6·2%).

1 : 2 : 3 : 4-*Tetrahydro*-5- *or* -7-*methoxy*-1 : 9-*dimethylcarbazole*; 1 : 2 : 3 : 4 : 10 : 11-*Hexahydro*-5- *and* -7-*methoxy*-9 : 11-*dimethylcarbazoles* (V and IV, respectively).—(*a*) A solution of crude *N*-methyl-*N*-nitroso-*m*-anisidine (17·2 g.) (from 40 g. of *N*-methyl-*m*-anisidine) in acetic acid (35 c.c.) was added dropwise to a stirred suspension of zinc dust (28 g.) in water (50 c.c.) at <10°; stirring was continued for a further 3 hr. The mixture was heated on the steam-bath, then filtered, and the residue washed with hot water and ether. The combined filtrate and washings were basified with sodium hydroxide solution and extracted with ether. Distillation of the very dark residue from the dried extract furnished a colourless oil (11 g.), b. p. 150°/8 mm., rapidly darkening in air. This crude hydrazine (10 g.) was heated on the steam-bath with 2-methyl*cyclo*hexanone (12 c.c.) and 30% acetic acid (1 c.c.) during 2 hr. A solution of concentrated sulphuric (11 c.c.) in water (180 c.c.) was added and the mixture heated on the steam-bath for 13 hr., cooled, and extracted with ether (A). The aqueous layer was basified and the liberated bases were extracted with ether (B). The residue from the dried and evaporated extract A was distilled, and the pale yellow oil (*ca.* 1 g.), b. p. 100—170°/0·5 mm., so obtained, was dissolved in light petroleum (b. p. 60—80°), passed through an alumina column (25 g.) and eluted with the same solvent. On evaporation, the eluates all afforded colourless crystals contaminated with a little oil. Recrystallisation from light petroleum gave 1 : 2 : 3 : 4-*tetrahydro*-5(or 7)-*methoxy*-1 : 9-*dimethylcarbazole* as colourless prisms, m. p. 107—108° (Found :

C, 78·3; H, 8·2. $C_{15}H_{19}ON$ requires C, 78·6; H, 8·4%). The dried extract B was distilled, giving a colourless oil, b. p. 85—130°/1 mm. (identified as *N*-methyl-*m*-anisidine) and a viscous oil (*ca.* 2 g.), b. p. 130—200°/1 mm. A solution of this product in ethanol (50 c.c.) was shaken under hydrogen at 40° with Raney nickel; 180 c.c. of hydrogen were absorbed. The ethanol was removed from the filtered solution, and the dark purple residue, in light petroleum (b. p. 40—60°), was chromatographed on alumina (60 g.). The eluate was collected in 50-c.c. portions, which were separately evaporated in a nitrogen stream. The first two fractions yielded small amounts (*ca.* 30 mg. each) of colourless crystals, m. p. 71—78°. Recrystallisation from light petroleum (b. p. 40—60°) furnished 1 : 2 : 3 : 4 : 10 : 11-*hexahydro-5-methoxy*-9 : 11-*dimethylcarbazole*, colourless plates, m. p. 83—84° (Found : C, 77·9; H, 9·3. $C_{15}H_{21}ON$ requires C, 77·9; H, 9·1%). The base, in dilute hydrochloric acid, gives a blood-red colour on addition of ferric chloride. Successive portions of the eluate, from the third to the tenth, provided decreasing quantities of a colourless oil, which gave a blood-red ferric reaction in dilute hydrochloric acid.

Fractions 11—19 inclusive did not contain any such base and the eluant was changed to light petroleum (b. p. 40—60°)–benzene (10 : 1).

Fractions 20—24 contained a trace of an oil which gave a bright red ferric reaction in dilute hydrochloric acid, but was insufficient for further investigation. The only other material eluted from the column was dark oil, obtained by the use of chloroform–benzene (1 : 1) as eluant. The residues from fractions 3—10 were combined and chromatographed from light petroleum (b. p. 40—60°) on alumina (*ca.* 20 g.), and eluted with the same solvent. The eluate was collected in 50-c.c. portions, which were evaporated in a nitrogen stream. Only two (successive) portions afforded any appreciable residues. These were combined and distilled; 1 : 2 : 3 : 4 : 10 : 11-*hexahydro*-7-*methoxy*-9 : 11-*dimethylcarbazole* was obtained as a colourless oil, b. p. 90—100° (bath)/0·05 mm. (Found : C, 78·2; H, 9·2. $C_{15}H_{21}ON$ requires C, 77·9; H, 9·1%).

(*b*) Similarly *N*-methyl-*m*-anisidine (75 g.) gave nitrosamine (90 g.), *N*-*m*-methoxyphenyl-*N*-methylhydrazine (48 g., crude, distilled) which was condensed with 2-methyl*cyclo*hexanone (30 c.c.) as above. The product was refluxed with acetic acid (350 c.c.) during 30 min. Acetic acid (280 c.c.) was removed by distillation under reduced pressure, and the residue added to 10% hydrochloric acid (550 c.c.). The ether extracts A and B were made as under (*a*), and A gave the tetrahydromethoxydimethylcarbazole, m. p. 107—108°, as before. The bases from extract B were distilled and gave liquid fractions, (i) b. p. 75—100°/0·1 mm., and (ii) b. p. 100—104°/0·1 mm. which were separately hydrogenated in ethanol at 50°, over Raney nickel. The solution of (i) absorbed 140 c.c. of hydrogen, and that of (ii) 830 c.c., and the products were isolated as oils. The product from (ii) was distilled and collected in two fractions, (iii) b. p. 75—95°/0·1 mm. (11·9 g.), and (iv) b. p. 95—115°/0·1 mm. (5·4 g.). The hydrogenation product of (i) (8·1 g.) was chromatographed on alumina (120 g.) and fractionally eluted with light petroleum (b. p. 40—60°). The eluate was collected in 50-c.c. fractions which were evaporated in a nitrogen stream. The 3rd, 4th, and 5th fractions left small amounts of solid residue, m. p. 72—80°. Succeeding fractions, to the 17th, gave a bright red colour with dilute hydrochloric acid and ferric chloride solution and left oils on evaporation. Fractions (iii) and (iv) from the distillation described above were treated in a manner similar to that described for fraction (i), and gave essentially similar results.

The crystals obtained from the first few portions of eluate from each of the three chromatograms were freed from adhering oil and washed with a little light petroleum (b. p. 40—60°). Crystallisation from the same solvent furnished 1 : 2 : 3 : 4 : 10 : 11-hexahydro-5-methoxy-9 : 11-dimethylcarbazole (2·3 g.), colourless prisms, m. p. 83—84°. The *picrate* formed yellow-green prisms, m. p. 152° (decomp.), from ethanol (Found : C, 55·4; H, 5·3; N, 11·9. $C_{15}H_{21}ON,C_6H_3O_7N_3$ requires C, 54·8; H, 5·3; N, 12·2%).

The oil and washings from the crystalline base, and the mother-liquors from its crystallisation, were combined with the oily residues from those fractions of the eluates which gave red colours in the ferric chloride tests. From the solution, by chromatographic methods similar to those described above, with activated alumina (200 g.) in a column 160 cm. in length, a small amount of the crystalline solid, m. p. 83—84°, was obtained and also a colourless oil, which was converted into a *picrate*, which formed yellow prisms (5·3 g.), m. p. 134—135° (decomp.), from ethanol (Found : C, 54·9; H, 5·1; N, 12·3. $C_{15}H_{21}ON,C_6H_3O_7N_3$ requires C, 54·8; H, 5·3; N, 12·2%). It was decomposed with ammonia and the liberated base isolated with ether, and twice distilled. 1 : 2 : 3 : 4 : 10 : 11-Hexahydro-7-methoxy-9 : 11-dimethylcarbazole (220 g.) was obtained as a colourless oil, b. p. 95—96°/0·03 mm. (Found : C, 78·0; H, 9·2; N, 6·4%).

Rhodamines.—The methoxylated bases were refluxed with concentrated aqueous hydrobromic acid for 2 hr. and the solution concentrated under diminished pressure to small volume.

Addition of water usually gave an oily, sometimes a crystalline, precipitate of a hydrobromide. The supernatant liquid was poured away and the salt (a very small portion sufficed) boiled with phthalic anhydride for about a minute. The melt was dissolved in alcohol. The liquid hexahydro-7-methoxy-9 : 11-dimethylcarbazole gave a dye which in colour and fluorescence closely matched Rhodamine B. The solid 5-methoxy-analogue gave a dye which was much bluer (purple) in acid alcoholic solution and exhibited a most intense *red* fluorescence, even on great dilution. Comparisons, which will be submitted later, indicate that this remarkable change in colour and fluorescence is probably due to the bulky (quaternary) group in the 2-position (vicinal to oxygen and nitrogen) of the *m*-aminophenol nucleus.

Rhodamine dyes are obtained in the manner described above from α-colubridine, strychnospermine, and dimethylharmine chloride after hydrogenation at an Adams catalyst, but not from β-colubridine, eserine, vomicidine, aspidospermine, or akuammine.

Oxidation of 1 : 2 : 3 : 4 : 10 : 11-*Hexahydro-6-methoxy-9* : 11-*dimethylcarbazole.*—1 : 2 : 3 : 4 : 10 : 11-Hexahydro-6-methoxy-9 : 11-dimethylcarbazole (2·0 g.) was dissolved in a mixture of water (150 c.c.) and 10% sulphuric acid (7 c.c.), and dilute sodium hydroxide solution was added to faint turbidity. The mixture was stirred at 50°, and a solution of potassium permanganate (6·5 g.) in water (110 c.c.), heated to 50°, was added during 15 min. Stirring was continued and after ½ hr., anhydrous sodium carbonate (1·0 g.) was added, and then a warm solution of potassium permanganate (5·0 g.) in water (100 c.c.) during 2 hr.; the permanganate colour then persisted. Anhydrous sodium carbonate (1·0 g.) was added, and stirring was continued at 50° for a further 2 hr. Sodium sulphite (0·2 g.) was added, and the mixture filtered; the manganese precipitate was washed with boiling water (250 c.c.). The combined filtrates were concentrated under reduced pressure to about 90 c.c., acidified with concentrated hydrochloric acid, and extracted with ether (8 × 15 c.c.). The ethereal solution was washed with water, dried, and concentrated. The residue was treated with ethereal diazomethane (from 5 g. of nitrosomethylurea) and kept overnight. The ether was evaporated, and the residue triturated with methanol, and filtered. The colourless residue was polymethylene, softening point 270°, insoluble in all the usual solvents (Found : C, 85·4; H, 13·9. Calc. for $[CH_2]_n$: C, 85·6; H, 14·4%). The filtrate was concentrated and the residue distilled, giving *substances* (*a*) b. p. 60—70°/0·03 mm. (Found : C, 59·1; H, 8·8; N, 2·4%), (*b*) b. p. 70—102°/0·03 mm. (Found : C, 60·5; H, 8·7; N, 4·0%), (*c*) b. p. 102—125° (bath)/0·03 mm. (Found : C, 62·5; H, 7·9; N, 5·4; OMe, 11·7; NMe, 6·0; *C*-Me, 4·7. $C_{14}H_{21}O_4N$ requires C, 62·9; H, 7·9; N, 5·2; OMe, 11·6; NMe, 10·9; *C*-Me, 5·8%).

γ-Methyl-α-oxobutyric Acid p-*Methoxyphenylhydrazone* (cf. Robinson and Suginome, *J.*, 1932, 298).—A solution of ethyl *iso*propylacetoacetate (20·6 g.) in ethanol (150 c.c.) at 0° was mixed with one of sodium hydroxide (12 g.) in water (30 c.c.). A solution of *p*-methoxybenzenediazonium chloride prepared from *p*-anisidine (12·4 g.), hydrochloric acid (50 c.c. of concentrated acid in 60 c.c. of water), and sodium nitrite (6·9 g.) in water (20 c.c.) was added immediately to the swirled and cooled (ice-bath) mixture. The heavy red oil which separated was isolated with ether after 6—7 min. and hydrolysed under reflux for 1 hr. with alcoholic 5% sodium hydroxide (165 c.c.). The solution was concentrated under diminished pressure, diluted with water (charcoal), washed twice with ether, boiled, cooled to 0°, and acidified with dilute hydrochloric acid. The yellow *hydrazone* was collected and dried (7·5 g.). It formed bright yellow needles, m. p. 129°, from light petroleum (b. p. 60—80°) or aqueous methanol (Found : C, 60·9; H, 6·9; N, 11·5. $C_{12}H_{14}O_3N_2$ requires C, 61·0; H, 6·8; N, 11·9%).

5-Methoxy-3 : 3-dimethylindolenine and 5-Methoxy-3 : 3-dimethylindolenine-2-carboxylic Acid.—A solution of γ-methyl-2-oxobutyric acid *p*-methoxyphenylhydrazone (3·6 g.) in ethanol (36 c.c.) was saturated with hydrogen chloride at 0°. The greenish-black mixture was refluxed for 5 min., and the ethanol was then removed at the room temperature under diminished pressure in a stream of nitrogen. The residue was shaken with ether and sodium carbonate solution. The aqueous layer was washed with ether, freed from ether under reduced pressure, cooled in ice, and acidified. The flocculent, colourless precipitate was collected, thoroughly washed with water, and dried (550 mg.). Three crystallisations from methanol, finally cooled to −40°, gave the *indolenine-acid* as colourless needles, m. p. 138—139° (Found : C, 65·3; H, 6·0. $C_{12}H_{13}O_2N$ requires C, 65·7; H, 6·0%).

The ethereal layer was washed with sodium carbonate solution and water, dried, and concentrated. The dark viscous residue was mixed with a few drops of methanol and kept at −5° for 4 days. The greenish solid was collected, washed with methanol and ether, and dried (1·3 g.). The product is very sparingly soluble in hot or cold methanol, ethanol, ether, and

light petroleum (b. p. 40—60°) but is easily soluble in benzene. Crystallisation from the latter solvent furnished *5-methoxy-3 : 3-dimethylindolenine* as colourless prisms, m. p. 123—124° (Found : C, 75·7; H, 7·5; N, 8·0. $C_{11}H_{13}ON$ requires C, 75·4; H, 7·5; N, 8·0%).

The attempted preparation of the methoxy-3 : 3-dimethylindolenine methiodide gave stout rods, m. p. 140—147°, which could not be recrystallised.

5-Methoxy-3 : 3-dimethylindolenine Methochloride.—A solution of the above indolenine (1·0 g.) and methyl sulphate (0·6 c.c.) in benzene (10 c.c.) was heated on the steam-bath for 15 min. The heavy brown oil which separated was washed with ether and treated with cold dilute potassium hydroxide, and the liberated base taken up in ether. The ethereal solution was washed with water, dried ($MgSO_4$), and filtered, and dry hydrogen chloride was passed in. The *methochloride* separated in large faintly brown prisms (0·78 g.), m. p. 166—167° (Found : C, 59·9; H, 7·7; N, 5·7; Cl, 14·4. $C_{12}H_{18}O_2NC$ lrequires C, 59·1; H, 7·5; N, 5·7; Cl, 14·5%)

5-Methoxy-1 : 3 : 3-trimethylindoline (VII).—A solution of the above methochloride (0·76 g.) and palladium chloride (1·3 c.c. of 1% solution) in methanol (40 c.c.) and concentrated hydrochloric acid (4 drops) was shaken in an atmosphere of hydrogen at room temperature and pressure. After 15 min. the solution had absorbed 73 c.c. of hydrogen, and in a further 30 min. 4 c.c. more of hydrogen were taken up, and absorption ceased. The filtered solution was concentrated to 10 c.c. under reduced pressure and then evaporated to dryness over concentrated sulphuric acid and potassium hydroxide in a vacuous desiccator. The residual mixture of crystals and a small amount of a yellow oil was washed with methanol, leaving *5-methoxy-1 : 3 : 3-trimethylindoline hydrochloride* (0·65 g.), colourless prisms, m. p. 207—208° (Found : C, 63·7; H, 8·1; N, 6·4. $C_{12}H_{17}ON$,HCl requires C, 63·3; H, 8·0; N, 6·2%). The hydrochloride (0·61 g.) was dissolved in water and basified with ammonia, and the liberated *base* isolated with ether and distilled as a colourless oil, b. p. 118° (bath)/5 mm. (Found : C, 75·7; H, 9·0; N, 7·2. $C_{12}H_{17}ON$ requires C, 75·4; H, 9·0; N, 7·3%).

1 : 2 : 3 : 4 : 10 : 11-Hexahydro-9 : 11-dimethylcarbazole.—(i) *as*-Methylphenylhydrazine (4·4 g.) was heated on a steam-bath with 2-methyl*cyclo*hexanone (5·5 c.c.), first at atmospheric pressure for ½ hr., and then under reduced pressure until no more water was removed. The product was refluxed with acetic acid (90 c.c.) during ½ hr., and most of the acetic acid (71 c.c.) was then removed under reduced pressure. Water (100 c.c.) and concentrated hydrochloric acid (7 c.c.) were added, the solution was extracted with ether and basified, and the liberated bases were isolated with ether and distilled *in vacuo*. A solution of the colourless oily distillate in ethanol (40 c.c.) was shaken in hydrogen at 40° with Raney nickel. Absorption ceased after about 500 c.c. of hydrogen had been taken up in 76 hr. Ethanol was removed from the filtered solution under diminished pressure and the residue was fractionated, giving a colourless oil (1·2 g.), b. p. 58—61°/2 mm., rapidly darkening in air, and then a colourless oil (4·3 g.), b. p. 122—124°/2 mm. The latter was converted into the *picrate* (8·4 g.) in ethanolic picric acid. After recrystallisation from ethanol, the derivative (7·8 g.) formed bright orange prisms, m. p. 135—136° (Found : C, 56·0; H, 5·1. $C_{14}H_{19}N,C_6H_3O_7N_3$ requires C, 55·8; H, 5·2%). The picrate (6·25 g.) was decomposed with ammonia solution, and the liberated *base* was isolated with ether and twice distilled; it was a colourless liquid (2·7 g.), b. p. 65°/0·005 mm. (Found : C, 83·8; H, 9·6. $C_{14}H_{19}N$ requires C, 83·5; H, 9·5%).

(ii) A mixture of 2 : 3 : 4 : 11-tetrahydro-11-methylcarbazole (1·0 g.), ether (10 c.c.), and methyl iodide (2 c.c.) was kept for 2 weeks. The brown prismatic crystals which separated were collected, once crystallised from ethanol, and dissolved in dilute hydrochloric acid. The solution was washed with ether and basified with ammonia, and the base isolated with ether and distilled as a colourless oil, b. p. 93—95° (bath)/0·05 mm. Its solution in ethanol (40 c.c.) was shaken for 4 days under hydrogen with Raney nickel. Working up as above gave a picrate which, once crystallised from ethanol, had m. p. 135—136°, unchanged on admixture with that obtained in (i) above.

1 : 2 : 3 : 4 : 10 : 11-Hexahydro-11-methylcarbazole.—A solution of 2 : 3 : 4 : 11-tetrahydro-11-methylcarbazole (1·15 g.) in ethanol (40 c.c.) was shaken under hydrogen at 35° with Raney nickel. After 3 days 160 c.c. of hydrogen had been taken up and absorption ceased. Ethanol was removed from the filtered solution under reduced pressure, and the residual *base* was distilled as a colourless oil (1·05 g.), b. p. 80—85° (bath)/0·03 mm. (Found : C, 83·4; H, 9·1; N, 7·7. $C_{13}H_{17}N$ requires C, 83·4; H, 9·2; N, 7·5%).

1 : 2 : 3 : 4-Tetrahydro-1 : 9-dimethylcarbazole.—*as*-Methylphenylhydrazine (10 c.c.) was heated on the steam-bath with 2-methyl*cyclo*hexanone (12 c.c.) for 1 hr. The product was refluxed with 10% sulphuric acid (200 c.c.) for 20 min., and allowed to cool. An ethereal solution of the oily layer was washed with dilute sulphuric acid and water. The oil from the dried extract

solidified on scratching and, twice crystallised from ethanol, the **1 : 2 : 3 : 4-*tetrahydro*-1 : 9-*dimethylcarbazole*** (6·55 g.) formed colourless plates, m. p. 57—59° (Found : C, 84·3; H, 8·7; N, 6·6. $C_{14}H_{17}N$ requires C, 84·4; H, 8·6; N, 7·0%).

1 : 2 : 3 : 4 : 10 : 11-*Hexahydro*-1 : 9-*dimethylcarbazole*.—A mixture of the tetrahydrodimethylcarbazole (5 g.), ethanol (40 c.c.), concentrated hydrochloric acid (20 c.c.), and granulated tin (25 g.) was refluxed on a steam-bath for 12 hr. The mixture was filtered hot, and the residue was washed with a hot mixture of ethanol (10 c.c.) and concentrated hydrochloric acid (10 c.c.). The combined filtrates and washings were cooled, basified with sodium hydroxide solution, and steam-distilled. The distillate was acidified with concentrated hydrochloric acid, filtered, twice washed with ether, and basified with ammonia, and the liberated *base* was isolated with ether and distilled, forming a colourless oil (2·3 g.), b. p. 100° (bath)/0·1 mm. (Found : C, 83·8; H, 9·6. $C_{14}H_{19}N$ requires C, 83·5; H, 9·5%). The *picrate*, yellow needles from ethanol, had m. p. 151—153° (Found : C, 55·9; H, 5·2; N, 13·4. $C_{14}H_{19}N,C_6H_3O_7N_3$ requires C, 55·8; H, 5·2; N, 13·0%).

1 : 2 : 3 : 4 : 10 : 11-*Hexahydro*-1-*methylcarbazole*.—A solution of **1 : 2 : 3 : 4**-tetrahydro-1-methylcarbazole (10 g.) (from phenylhydrazine and 2-methyl*cyclo*hexanone) in ethanol (40 c.c.) and concentrated hydrochloric acid (25 c.c.) along with granulated tin (20 g.) was refluxed for 12 hr. The *base* was isolated as a colourless oil (4·3 g.), b. p. 85° (bath)/0·05 mm. (Found : C, 83·7; H, 9·3. $C_{13}H_{17}N$ requires C, 83·4; H, 9·2%). The *picrate* crystallised from benzene in bright, orange-red prisms, m. p. 151—153° (Found : C, 54·5; H, 5·1. $C_{13}H_{17}N,C_6H_3O_7N_3$ requires C, 54·8; H, 4·8%).

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DYSON PERRINS LABORATORY, OXFORD. [*Received, April 20th*, 1955.]

Triterpenoids. Part XLIII. The Constitution of Some Compounds obtained by the Dehydration of α-Amyrin and Related Alcohols.*

By G. G. ALLAN, F. S. SPRING, ROBERT STEVENSON, and W. S. STRACHAN.

[Reprint Order No. 6335.]

The hydrocarbon, "*d*-α-amyradiene," obtained by the dehydration of α-amyrin (I) by using phosphorus pentachloride, is shown to be **8 : 10 : 14**-trimethyl-5ξ-novursa-**3(4) : 12**-diene (V), since it is obtained by Wolff–Kishner reduction of **8 : 10 : 14**-trimethyl-5ξ-novursa-**3(4) : 12**-dien-**11**-one (III) and when ozonised it gives acetone and the ketone (IV). The **3(4) : 12**-diene (V) is isomerised by trichloroacetic acid to the **3(5) : 12**-diene (V*a*), also obtained by Wolff–Kishner reduction of the αβ-unsaturated ketone (VI). The oxo-diene, "α-amyradienone-III," obtained by dehydration of **11**-oxours-**12**-en-**3β**-ol (II) with hydriodic acid is **5 : 8 : 14**-trimethylnovursa-**9(10) : 12**-dien-**11**-one (X). Dehydration of ursa-**9(11) : 12**-dien-**3β**-ol (XIII) with phosphorus pentachloride gives a hydrocarbon, "*d*-α-amyratriene," identified as **8 : 10 : 14**-trimethyl-5ξ-novursa-**3(4) : 9(11) : 12**-triene (XIV). **5 : 8 : 14**-Trimethylnovursa-**1(10) : 9(11) : 12**-triene (XV) is obtained from **5 : 8 : 14**-trimethylnovursa-**9(10) : 12**-dien-**11**-one (X) by treatment with lithium aluminium hydride. An isomeric triene, "*l*-α-amyratriene," previously obtained by dehydration of the alcohol (XIII) with phosphoric oxide, is also obtained from the triene (XV) by the action of mineral acid and is considered to be **5 : 8 : 14**-trimethylnovursa-**9(10) : 11 : 13(18)**-triene (XVI).

THE experiments described in this and the following paper were designed to determine the constitution of a number of products obtained by the dehydration of α-amyrin (I) and related compounds. Dehydration of 3β-hydroxyurs-12-en-11-one (II) with phosphorus

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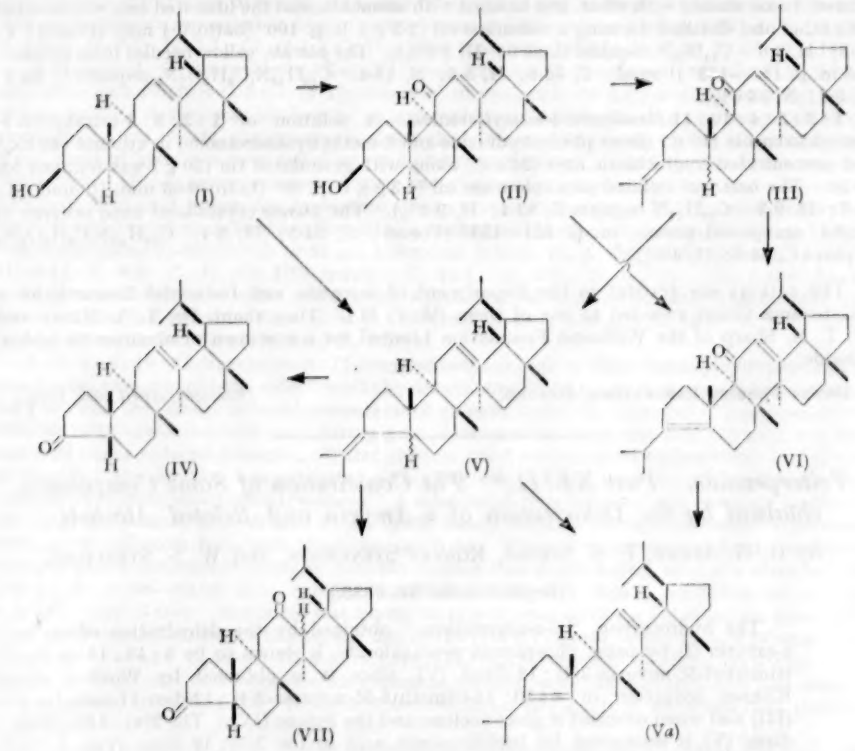
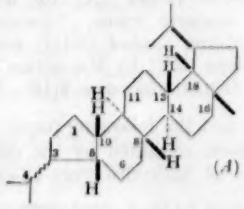
pentachloride gives a mixture of two oxo-dienes (Spring and Vickerstaff, *J.*, 1937, 249), identified as 8 : 10 : 14-trimethyl-5ξ-novursa-3(4) : 12-dien-11-one (" α-amyradienone-I ") (III) and 8 : 10 : 14-trimethylnovursa-3(5) : 12-dien-11-one (" α-amyradienone-II ") (VI) * (Ruzicka, Jeger, and Volli, *Helv. Chim. Acta*, 1945, **28**, 767, 1628). Ruzicka *et al.* (*loc. cit.*) showed that when the oxo-diene (III) is shaken with hydrogen and a palladium catalyst, it is converted into the isomer (VI); we find that the same isomerisation is brought about by treatment of (III) with hydrochloric–acetic acid. Many examples of similar ring A contractions accompanying ionic-type dehydrations of 3β-hydroxy-triterpenoids have



since been described (for references, see Jeger, " Fortschritte der Chemie organischen Naturstoffe," Springer-Verlag, 1950, Vol. VII, p. 1).

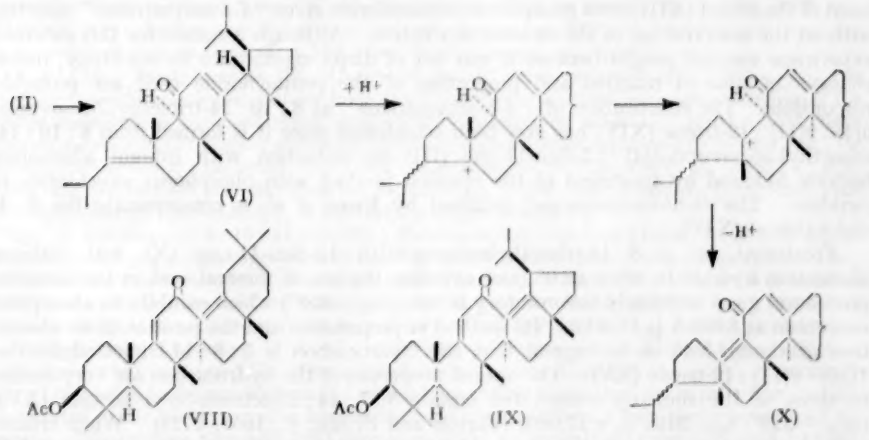
Dehydration of α-amyrin (I) with phosphorus pentachloride yields " *d*-α-amyradiene " (Vesterberg and Westerlind, *Annalen*, 1922, **428**, 250), which does not show selective

* As a basis for a more systematic nomenclature of the dehydration products described in this and the following paper, the hydrocarbon, $C_{27}H_{44}$, having the constitution and stereochemistry represented by (*A*) is called novursane.



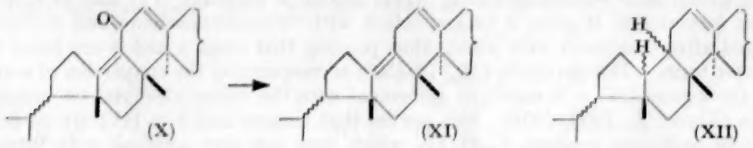
absorption of high intensity above 2200 Å (Ewen, Gillam, and Spring, *J.*, 1944, 28). This hydrocarbon has now been identified as 8 : 10 : 14-trimethyl-5ξ-novursa-3(4) : 12-diene (V). This identification is supported by the following facts. First, the diene (V) is obtained from 8 : 10 : 14-trimethyl-5ξ-novursa-3(4) : 12-dien-11-one (III) by Wolff–Kishner reduction. Again, when treated with ozone it gives acetone, a compound, $C_{27}H_{42}O$, and a very small quantity of a compound $C_{27}H_{42}O_2$. The infrared absorption spectrum of the compound $C_{27}H_{42}O$ includes a strong band at 1740 cm.$^{-1}$ (in CCl_4) and consequently it contains a ketone group in a 5-membered ring. This ketone is therefore (IV) and in agreement with this formulation it gives a yellow colour with tetranitromethane and is recovered unchanged after treatment with alkali, thus proving that rings A and B are fused in the more stable form. The change in $[M_D]$ (+450°) accompanying the conversion of α-amyrin (I) into the ketone (IV) is in excellent agreement with the values observed for comparable reactions (Klyne, *J.*, 1952, 2916); this proves that rings A and B in (IV) are *cis*-β-fused. The second oxidation product, $C_{27}H_{42}O_2$, which does not give a colour with tetranitromethane, is considered to be the diketone (VII). Treatment of the diene (V) with trichloroacetic acid in chloroform gives the isomeric 8 : 10 : 14-trimethylnovursa-3(5) : 12-diene (V*a*), the structure of which follows from its formation by Wolff–Kishner reduction of 8 : 10 : 14-trimethylnovursa-3(5) : 12-dien-11-one (VI).

Dehydration of 3β-hydroxyurs-12-en-11-one (II) with hydriodic–acetic acid gives a third dienone, " α-amyradienone-III " (Ewen *et al.*, *loc cit.*) which, we find, can also be obtained by treatment of 8 : 10 : 14-trimethylnovursa-3(5) : 12-dien-11-one (IV) with hydriodic–acetic acid. The ultraviolet absorption spectrum of " α-amyradienone-III " shows maxima at 2040, 2580, and 2900 Å (ε 9900, 11,000, and 10,200) and in this respect closely resembles that of 12-oxo-oleana-9(11) : 13(18)-dien-3β-yl acetate (VIII) (Beaton, Johnston, McKean, and Spring, *J.*, 1953, 3660) and 12-oxoursa-9(11) : 13(18)-dien-3β-yl acetate (IX) (Beaton, Shaw, Spring, Stevenson, Strachan, and Stewart, *J.*, 1955, 2606), the characteristic absorption spectra of which have been related to the geometry of the ·C:C·CO·C:C chromophore. It follows that " α-amyradienone-III " contains a similarly constrained chromophore and that it is 5 : 8 : 14-trimethylnovursa-9(10) : 12-dien-11-one (X); its formation from 8 : 10 : 14-trimethylnovursa-3(5)-12-dien-11-one (VI) is represented in the annexed formulæ :



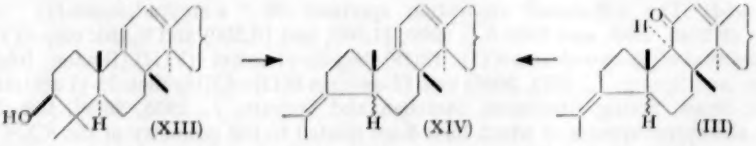
Reduction of 5 : 8 : 14-trimethylnovursa-9(10) : 12-dien-11-one (X) either by the Wolff–Kishner method or by prolonged refluxing with lithium aluminium hydride in ether gives a non-conjugated diene, 5 : 8 : 14-trimethylnovursa-9(10) : 12-diene (XI) which shows strong ethylenic absorption in the region 2100—2200 Å and gives a strong positive reaction with tetranitromethane. This behaviour of the 11-oxo-9(10) : 12-diene (X) is similar to

that of the oxo-diene (VIII). In one respect, however, the behaviour of 5 : 8 : 14-trimethylnovursa-9(10) : 12-dien-11-one (X) differs from that of 12-oxo-oleana-9(11) : 13(18)-dien-3β-yl acetate and of 12-oxoursa-9(11) : 13(18)-dien-3β-yl acetate (IX). Catalytic hydrogenolysis of each of the last two compounds gives the corresponding non-conjugated diene, whereas similar treatment of the oxo-diene (X) results in the absorption of 3 mols. of hydrogen and the formation of a monoethylenic hydrocarbon, the optical properties of which suggest that it may be 5 : 8 : 14-trimethyl-9ξ : 10ξ-novurs-12-ene (XII).



(X) (XI) (XII)

Treatment of 5 : 8 : 14-trimethylnovursa-9(10) : 12-diene (XI) with hydrochloric–acetic acid gives the conjugated "*l*-α-amyradiene" previously obtained by treatment of α-amyrin with phosphoric oxide (Vesterberg, *Ber.*, 1891, **24**, 3835; Ewen *et al.*, *loc. cit.*) and the constitution of this is discussed in the following paper. "*l*-α-Amyradiene" is also obtained from 8 : 10 : 14-trimethyl-5ξ-novursa-3(4) : 12-diene (V) by treatment with boron trifluoride–acetic acid.

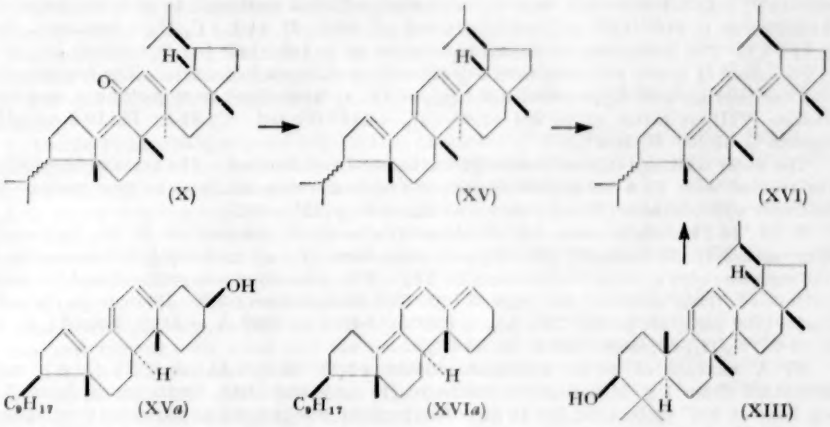


(XIII) (XIV) (III)

Dehydration of ursa-9(11) : 12-dien-3β-ol (XIII) with phosphorus pentachloride gives a dichloro-α-amyradiene, which with zinc yields "*d*-α-amyratriene"; the ultraviolet absorption spectrum of this shows that the double bond introduced by the dehydration is remote from the conjugated system in ring C (Ewen *et al.*, *loc. cit.*). In our hands, treatment of the dienol (XIII) with phosphorus pentachloride gives "*d*-α-amyratriene" directly, without the intervention of the dichloro-derivative. Although a reason for this different experience was not sought because it was not of direct significance to our study, minor changes in time of reaction and proportion of the pentachloride used are probably responsible. The constitution of "*d*-α-amyratriene" as 8 : 10 : 14-trimethyl-5ξ-novursa-3(4) : 9(11) : 12-triene (XIV) has now been established since it is formed from 8 : 10 : 14-trimethyl-5ξ-novursa-3(4) : 12-dien-11-one (III) by reduction with lithium aluminium hydride followed by treatment of the reaction product with phosphorus oxychloride in pyridine. The dichloro-compound obtained by Ewen *et al.* is consequently the 3 : 4-dichloride of (XIV).

Treatment of 5 : 8 : 14-trimethylnovursa-9(10) : 12-dien-11-one (X) with lithium aluminium hydride in ether at 0° (and avoiding the use of mineral acid in the isolation procedure) gives a strongly lævorotatory triene ($[\alpha]_D$ −358°) which exhibits an absorption maximum at 3200 Å (ε 15,000). Its method of preparation and the position of its absorption maximum lead us to suggest that this hydrocarbon is 5 : 8 : 14-trimethylnovursa-1(10) : 9(11) : 12-triene (XV). The optical properties of the hydrocarbon are very similar to those of the similarly constituted ergosta-5 : 7 : 14 : 22-tetraen-3β-yl acetate (XV*a*) ($[\alpha]_D$ −322°, $\lambda_{max.}$ 3190 Å, ε 15,000) (Barton and Bruun, *J.*, 1951, 2728). When treated with hydrochloric–acetic acid, 5 : 8 : 14-trimethylnovursa-1(10) : 9(11) : 12-triene (XV) yields "*l*-α-amyratriene," previously obtained by dehydration of ursa-9(11) : 12-dien-3β-ol (XIII) by phosphoric oxide (Ewen *et al.*, *loc. cit.*). "*l*-α-Amyratriene" is strongly lævorotatory and exhibits a triple-maxima absorption spectrum, the principal band in which is at 2950 Å (ε 35,000). These properties are best explained if "*l*-α-amyratriene" is 5 : 8 : 14-trimethylnovursa-9(10) : 11 : 13(18)-triene (XVI) (cf. Beton and Halsall, *Chem.*

and Ind., 1954, 1560). Ergosta-4 : 6 : 8(14) : 22-tetraene (XVI*a*), which contains a chromophore comparable with that in (XVI), has similar absorption ($\lambda_{max.}$ 2830 Å, ε 33,000) (Fieser, Rosen, and Fieser, *J. Amer. Chem. Soc.*, 1952, **74**, 5397). The calculated value



(2940 Å) for the location of the absorption maximum of the triene (XVI), on the basis of Woodward's empirical rules, is in excellent agreement with the observed value.

Experimental

Rotations were measured in $CHCl_3$ and ultraviolet absorption spectra in EtOH solutions. Grade II alumina and light petroleum, b. p. 60—80°, were used for chromatography.

8 : 10 : 14-Trimethyl-5ξ-novursa-3(4) : 12-dien-11-one (" α-amyradienone-I ") was prepared by the action of phosphorus pentachloride on 3β-hydroxyurs-12-en-11-one (II). Crystallisation from chloroform–methanol gave the oxo-diene (yield, 60%) as needles, m. p. 197—199°, $[\alpha]_D$ +167° (*c*, 2·9). Spring and Vickerstaff (*loc. cit.*) give m. p. 197°, $[\alpha]_D$ +166°, and Ruzicka, Jeger, and Volli (*loc. cit.*) give m. p. 199—200° (high vacuum), $[\alpha]_D$ +167°.

8 : 10 : 14-*Trimethylnovursa*-3(5) : 12-*dien*-11-*one* (" α-*Amyradienone*-II ") (VI).—(*a*) The chloroform–methanol mother-liquors from the 11-oxo-3(4) : 12-diene were evaporated, and the residue dissolved in light petroleum and chomatographed on alumina. Elution with light petroleum–benzene (3 : 1) gave a fraction which crystallised from methanol to yield 8 : 10 : 14-trimethylnovursa-3(5) : 12-dien-11-one (10%) as needles, m. p. 155—156°, $[\alpha]_D$ +147° (*c*, 0·8). Spring and Vickerstaff (*loc. cit.*) give m. p. 156°, $[\alpha]_D$ +153°, and Ruzicka, Jeger, and Volli (*loc. cit.*) give m. p. 154—155°, $[\alpha]_D$ +149° for " α-amyradienone-II."

(*b*) A solution of 8 : 10 : 14-trimethyl-5ξ-novursa-3(4) : 12-dien-11-one (III) (0·5 g.) in acetic acid (50 c.c.) containing concentrated hydrochloric acid (5 c.c.) was refluxed for 16 hr., with addition of concentrated hydrochloric acid (2 c.c.) every 4 hr. The product was isolated in the usual way and crystallised from methanol, to give the 11-oxo-3(5) : 12-diene (0·3 g.) as prismatic needles, m. p. 153—154° (no depression), $[\alpha]_D$ +149° (*c*, 1·7), $\lambda_{max.}$ 2520 Å (ε 13,000).

Wolff–Kishner Reduction of 8 : 10 : 14-*Trimethyl*-5ξ-*novursa*-3(4) : 12-dien-11-*one* (III).—A mixture of the oxo-diene (III) (800 mg.), sodium methoxide (from 1 g. of sodium) in methanol (15 c.c.) and 100% hydrazine hydrate (5 c.c.) was kept at 200° (autoclave) for 15 hr. The product was isolated in the usual way, dissolved in light petroleum (100 c.c.), and chromatographed on alumina. The fraction eluted by light petroleum (200 c.c.) crystallised from methanol, to yield 8 : 10 : 14-trimethyl-5ξ-novursa-3(4) : 12-diene (V) (310 mg.) as prisms, m. p. 134—135°, $[\alpha]_D$ +109° (*c*, 1·3), undepressed in m. p. when mixed with a sample of " *d*-α-amyradiene," m. p. 133—135°, $[\alpha]_D$ +110°, prepared by the method of Vesterberg and Westerlind (*loc. cit.*).

Ozonolysis of 8 : 10 : 14-*Trimethyl*-5ξ-*novursa*-3(4) : 12-*diene* (V).—A solution of the diene (V) (1·0 g.) in chloroform (200 c.c.) was treated at −35° with ozone (2 mols.). After attaining room temperature the mixture was stirred with zinc dust (3 g.) and acetic acid (50 c.c.) for 1 hr.

The filtered solution was washed with water (5 × 250 c.c.; see below), the chloroform evaporated, and the residue triturated with methanol whereupon it crystallised. Two recrystallisations from methanol yielded a mixture (350 mg.), a solution of which in light petroleum was chromatographed on alumina. Light petroleum eluted a fraction (250 mg.; m. p. 146—147°, $[\alpha]_D$ +205°) which was thrice crystallised from methanol, to give the *ketone* (IV), as needles, m. p. 146—148°, $[\alpha]_D$ +210° (Found : C, 84·9; H, 11·1. $C_{27}H_{42}O$ requires C, 84·75; H, 11·1%). The ketone was recovered unchanged, m. p. 145—147° (no depression), $[\alpha]_D$ +201° (*c*, 0·5), after 2½ hours' refluxing with 5% ethanolic potassium hydroxide. The fraction eluted from the column with light petroleum–benzene (2 : 1) crystallised from methanol, to give the *dikctone* (VII), as plates, m. p. 204—206°, $[\alpha]_D$ +184° (Found : C, 81·8; H, 10·6. $C_{27}H_{42}O_2$ requires C, 81·35; H, 10·6%).

The water washings (above) were adjusted to pH 7 and distilled. The first fraction (200 c.c.) was treated with 2 : 4-dinitrophenylhydrazine hydrochloride solution, to give acetone 2 : 4-dinitrophenylhydrazone (25 mg.), m. p. and mixed m. p. 121—124°.

8 : 10 : 14-*Trimethylnovursa*-3(5) : 12-*diene* (V*a*).—(*a*) A solution of 8 : 10 : 14-trimethyl-5ξ-novursa-3(4) : 12-diene (V) (700 mg.) in chloroform (7 c.c.) containing trichloroacetic acid (700 mg.) was kept at room temperature for 1 hr. The chloroform was removed and the product crystallised from acetone, to yield 8 : 10 : 14-*trimethylnovursa*-3(5) : 12-*diene* as hexagonal prisms (200 mg.), m. p. 70—72°, $[\alpha]_D$ +123° (*c*, 1·4), ε at 2080 Å = 4500 (Found : C, 87·8; H, 11·9. $C_{30}H_{48}$ requires C, 88·2; H, 11·8%).

(*b*) A mixture of 8 : 10 : 14-trimethylnovursa-3(5) : 12-dien-11-one (VI) (1 g.), sodium methoxide (from 1 g. of sodium) in methanol (15 c.c.), and 100% hydrazine hydrate (5 c.c.) was kept at 200° (autoclave) for 15 hr. The product was isolated in the usual way, dissolved in light petroleum (50 c.c.), and chromatographed on alumina. The fraction eluted by petroleum (200 c.c.) was crystallised from acetone, to yield 8 : 10 : 14-trimethylnovursa-3(5) : 12-diene as prisms (200 mg.), m. p. 68—69° (no depression), $[\alpha]_D$ +120° (*c*, 2·1).

5 : 8 : 14-*Trimethylnovursa*-9(10) : 12-*dien*-11-*one* (α-*Amyradienone*-III) (X).—(*a*) Treatment of 3β-hydroxyurs-12-en-11-one (II) with hydriodic acid in acetic acid as described by Ewen *et al.* (*loc. cit.*) gave 5 : 8 : 14-trimethylnovursa-9(10) : 12-dien-11-one (X) as large laminæ (from methanol), m. p. 170—171°, $[\alpha]_D$ +171° (*c*, 3·3), $\lambda_{max.}$ 2040, 2580, and 2900 Å (ε 9900, 11,000, and 10,200). It gives a yellow colour with tetranitromethane. Ewen *et al.* (*loc. cit.*) give m. p. 169°, $[\alpha]_D$ +170°. Similar treatment of 11-oxours-12-en-3β-yl acetate or benzoate gave the oxo-diene (X) in approximately the same yield.

(*b*) Hydriodic acid (*d*, 1·7; 5 c.c.) was added to a solution of 8 : 10 : 14-trimethylnovursa-3(5) : 12-dien-11-one (VI) (2 g.) in glacial acetic acid (10 c.c.) and the mixture refluxed for 8 hr. The product was isolated in the usual way and crystallised from methanol, to yield 5 : 8 : 14-trimethylnovursa-9(10) : 12-dien-11-one as laminæ (1·2 g.), m. p. 170—172° (no depression), $[\alpha]_D$ +172° (*c*, 2·1).

5 : 8 : 14-*Trimethylnovursa*-9(10) : 12-*diene* (XI).—(*a*) A solution of 5 : 8 : 14-trimethylnovursa-9(10) : 12-dien-11-one (X) (1·0 g.) in ether (500 c.c.) was refluxed with lithium aluminium hydride (1 g.) for 7 hr. After 16 hr. at room temperature, the mixture was worked up in the usual way and the product crystallised from acetone–methanol, to give 5 : 8 : 14-*trimethylnovursa*-9(10) : 12-*diene* (XI) (560 mg.) as plates m. p. 98—99°, $[\alpha]_D$ +120° (*c*, 2·8), ε at 2080 Å = 13,200 (Found : C, 87·95; H, 11·9. $C_{30}H_{48}$ requires C, 88·2; H, 11·8%). It gives an orange colour with tetranitromethane.

(*b*) A mixture of 5 : 8 : 14-trimethylnovursa-9(10) : 12-dien-11-one (X) (1·0 g.), sodium methoxide (from 1 g. of sodium) in methanol (15 c.c.), and 100% hydrazine hydrate (5 c.c.) was kept at 200° (autoclave) for 15 hr. The product crystallised from methanol, to yield 5 : 8 : 14-trimethylnovursa-9(10) : 12-diene (XI) (250 mg.) as plates, m. p. 94—96° (no depression), $[\alpha]_D$ +118° (*c*, 0·9), ε at 2080 Å = 12,000.

Catalytic Hydrogenation of 5 : 8 : 14-*Trimethylnovursa*-9 : 12-*dien*-11-*one* (X).—A solution of the oxo-diene (X) (600 mg.) in glacial acetic acid (100 c.c.) was shaken with platinum (from 250 mg. of PtO_2) and hydrogen for 24 hr. The product was isolated in the usual manner and crystallised from acetone–methanol, to give 5 : 8 : 14-*trimethyl*-9ξ : 10ξ-*novurs*-12-*ene* (XII) (350 mg.) as plates, m. p. 95—96°, $[\alpha]_D$ +140° (*c*, 1·4), ε at 2060 Å = 2750 (Found : C, 87·7; H, 12·3. $C_{30}H_{50}$ requires C, 87·8; H, 12·2%). It gives a yellow colour with tetranitromethane; a mixture with (XI) had m. p. 65—73°.

Treatment of 5 : 8 : 14-*Trimethylnovursa*-9(10) : 12-*diene* (XI) *with Hydrochloric Acid.*—A solution of the 9(10) : 12-diene (150 mg.) in chloroform (5 c.c.) and acetic acid (50 c.c.) containing concentrated hydrochloric acid (10 c.c.) was refluxed for 16 hr. with the addition of

concentrated hydrochloric acid (2 c.c.) every 2 hr. The product was isolated in the usual way and crystallised from chloroform–methanol, to give "*l*-α-amyradiene" (50 mg.) as plates, m. p. 193—194° (no depression), $[\alpha]_D$ −110° (*c*, 1·9), $\lambda_{max.}$ 2360, 2410, and 2500 Å (ε 13,200, 14,500, and 8550).

Treatment of 8 : 10 : 14-*Trimethyl*-5ξ-*novursa*-3(4) : 12-*diene* (V) *with Boron Trifluoride.*—A solution of the 3(4) : 12-diene (V) (250 mg.) in glacial acetic acid (100 c.c.) and boron trifluoride–acetic acid (3 c.c.) was refluxed for 80 hr. The product was isolated through ether and crystallised from chloroform–methanol, to give "*l*-α-amyradiene" as plates (130 mg.), m. p. 193—194° (no depression), $[\alpha]_D$ −104° (*c*, 1·5), $\lambda_{max.}$ 2360, 2410, and 2500 Å (ε 13,000, 14,500, and 8500).

8 : 10 : 14-*Trimethyl*-5ξ-*novursa*-3(4) : 9(11) : 12-*triene* ("d-α-*Amyratriene*") (XIV).—(*a*) A solution of 8 : 10 : 14-trimethyl-5ξ-novursa-3(4) : 12-dien-11-one (III) (500 mg.) in ether (200 c.c.) was refluxed with lithium aluminium hydride (500 mg.) for 3 hr. A solution of the product (isolated in the usual way) in pyridine (50 c.c.) was refluxed for 15 hr. with phosphorus oxychloride (20 c.c.). The product crystallised from methanol, from which 8 : 10 : 14-trimethyl-5ξ-novursa-3(4) : 9(11) : 12-triene separated as needles (200 mg.), m. p. 132—133°, $[\alpha]_D$ +445° (*c*, 2·1). Ewen *et al.* (*loc. cit.*) give m. p. 131—133°, $[\alpha]_D$ +439°.

(*b*) A solution of ursa-9(11) : 12-dien-3β-ol (3·0 g.) in light petroleum (b. p. 60—80°; 80 c.c.) was shaken with phosphorus pentachloride (1·47 g.) for 1½ hr. After refluxing for 2 min., the mixture was treated with water and the product isolated in the usual way. Crystallisation from methanol–chloroform gave 8 : 10 : 14-trimethyl-5ξ-novursa-3(4) : 9(11) : 12-triene as needles, m. p. 132—134° (no depression), $[\alpha]_D$ +439° (*c*, 0·9), $\lambda_{max.}$ 2780 Å (ε 9500) (Found : C, 88·4; H, 11·5. Calc. for $C_{30}H_{48}$: C, 88·6; H, 11·4%)

5 : 8 : 14-*Trimethylnovursa*-1(10) : 9(11) : 12-*triene* (XV).—A solution of 5 : 8 : 14-trimethylnovursa-9(10) : 12-dien-11-one (X) in dry ether (200 c.c.) was treated with lithium aluminium hydride at 0° and kept at this temperature for 72 hr. The product was isolated, the use of mineral acid being avoided, and crystallised from methanol, to yield 5 : 8 : 14-*trimethylnovursa*-1(10) : 9(11) : 12-*triene* (300 mg.) as needles, m. p. 145—146°, $[\alpha]_D$ −358° (*c*, 1·6), $\lambda_{max.}$ 3200 Å (ε 15,000) (Found : C, 88·8; H, 11·4%).

5 : 8 : 14-*Trimethylnovursa*-9(10) : 11 : 13(18)-*triene* ("l-α-*Amyratriene*") (XVI).—A solution of the 1(10) : 9(11) : 12-triene (XV) (80 mg.) in acetic acid containing concentrated hydrochloric acid (2 c.c.) was heated at 100° for 2 hr. and then kept at room temperature for 48 hr. The mixture was again heated on the steam-bath for 3 hr. and the product isolated in the usual way. Crystallisation from methanol yielded 5 : 8 : 14-trimethylnovursa-9(10) : 11 : 13(18)-triene (50 mg.) as needles, m. p. 140—142°, $[\alpha]_D$ −450° (*c*, 0·5), $\lambda_{max.}$ 2860 (shoulder) 2950, and 3080 (shoulder) Å (ε 28,200, 33,800, and 24,500). A specimen perpared as described by Ewen *et al.* (*loc. cit.*) had m. p. and mixed m. p. 140—142°, $[\alpha]_D$ −455° (*c*, 3·1), $\lambda_{max.}$ 2860 (shoulder), 2950, and 3080 (shoulder) Å (ε 30,200, 35,500, and 25,500).

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Triterpenoids. Part XLIV. The Constitution of "l-α-Amyradiene."*

By M. B. E. Fayez, James Grigor, F. S. Spring, and Robert Stevenson.

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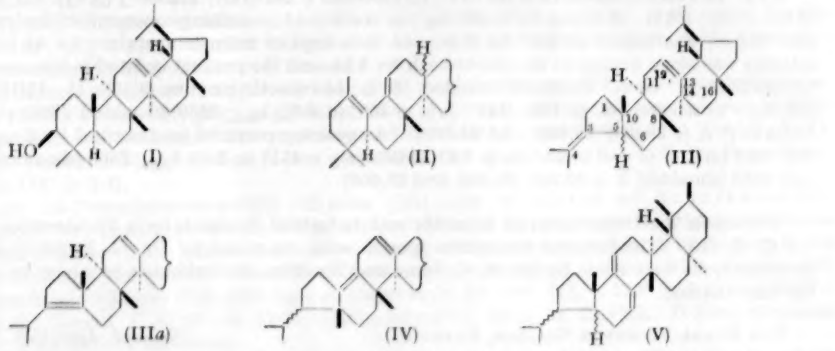
The hydrocarbon, "*l*-α-amyradiene," obtained by dehydration of α-amyrin (I) with either phosphoric oxide or hydriodic acid (or by treatment of α-amyrin acetate with the latter reagent), is shown to be 5 : 8α : 9β-trimethyl-10α-novursa-12 : 14-diene (XIV). Neither the 3(4) : 12-diene (III) nor the 3(5) : 12-diene (III*a*) is an intermediate in the phosphoric oxide reaction since these hydrocarbons are not isomerised by this reagent. The formation of the "*l*-diene" (XIV) from α-amyrin is considered to be a fully concerted reaction and it includes the migration of three axial methyl groups.

Elucidation of the constitution of the "*l*-diene" was facilitated by a study of the action of hydriodic acid on 12-oxoursanyl acetate (VI) which gives an αβ-unsaturated ketone identified as 5 : 8α : 9β-trimethyl-10α-novurs-13-en-12-one (XIII). This αβ-unsaturated ketone is also obtained from the "*l*-diene" and, conversely, it is converted into the "*l*-diene" by reduction with lithium aluminium hydride followed by treatment with mineral acid. The position of the double bond in the αβ-unsaturated ketone (XIII) was disclosed by its optical properties and by its oxidation to the transoid ene-dione, 5 : 8α : 9β-trimethyl-10α-novurs-13-ene-12 : 15-dione (XVII).

Dehydration of α-amyrin (I) by phosphoric oxide in benzene at room temperature gives, in high yield, a hydrocarbon, "*l*-α-amyradiene," in which the two double bonds are conjugated and heteroannular. The diene is also obtained by treatment of α-amyrin or its acetate with hydriodic–acetic acid (Vesterberg, *Ber.*, 1891, **24**, 3835; Ewen, Gillam, and Spring, *J.*, 1944, 28). A structure (II),† provisionally attributed to the hydrocarbon by



Ewen, Gillam, and Spring (*loc. cit.*), became improbable with the subsequent proof that ionic-type dehydrations of 3β-hydroxy-triterpenoids contract ring A (for references see Jeger, "Fortschritte der Chemie organischer Naturstoffe," Springer-Verlag, 1950, Vol. VII, p. 1) and it has since been excluded by the preparation of the "*l*-diene" by the isomerisation of two hydrocarbons, each of which contains a contracted ring A. Treatment of 8 : 10 : 14-trimethyl-5ξ-novursa-3(4) : 12-diene (III)‡ with boron trifluoride and of 5 : 8 : 14-trimethylnovursa-9(10) : 12-diene (IV) with hydrochloric–acetic acid gives the "*l*-diene" (preceding paper). Recently it has been suggested that the constitution of the "*l*-diene" is to be represented by (V) (Beton and Halsall, *Chem. and Ind.*, 1954, 1560).

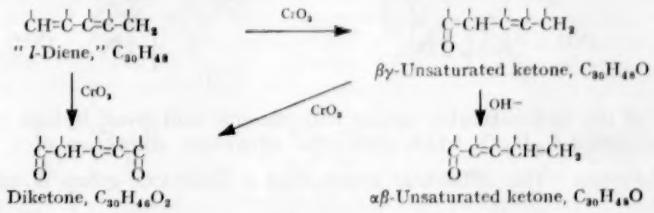
* Part XLIII, preceding paper.

† This formula is translated to correspond with that (I) recently proposed for α-amyrin (Beaton, Spring, Stevenson, and Strachan, *J.*, 1955, 2610).

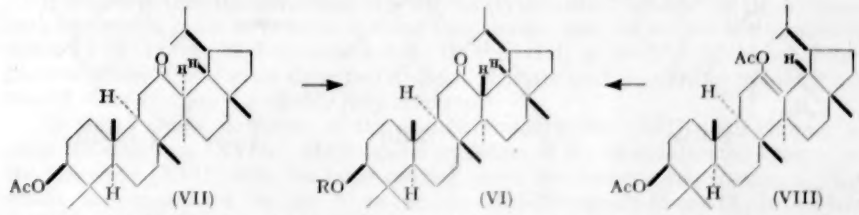
‡ The nomenclature adopted for ring A contracted ursane derivatives is explained in the preceding paper.

Irrespective of the constitution ascribed the ring E, this structure likewise cannot be correct for reasons which will become clear in the sequel.

Oxidation of the "*l*-diene," $C_{30}H_{48}$, with chromic acid (*ca.* 1·5 atoms of oxygen) yields a compound, $C_{30}H_{48}O$, which does not show high-intensity ultraviolet absorption above 2200 Å. The presence of an isolated double bond in the compound is shown by its positive tetranitromethane reaction and by its ultraviolet absorption, the intensity of which suggests that the double bond is of the type $>C{:}CH-$. The infrared absorption spectrum of the compound, $C_{30}H_{48}O$, contains a strong band at 1698 cm.$^{-1}$, thus showing that the oxygen function is an isolated ketone group in a 6-membered ring. Although the compound is stable to acid, when treated with alkali it gives an αβ-unsaturated ketone ($\lambda_{max.}$ 2600 Å, ε 9000). These properties and its origin show that the primary oxidation product of the "*l*-diene" is a βγ-unsaturated ketone. More drastic oxidation of either the "*l*-diene" or the βγ-unsaturated ketone with chromic acid gives a compound $C_{30}H_{46}O_2$, which contains an αβ-unsaturated ketone function ($\lambda_{max.}$ 2500 Å, ε 10,500) and a second isolated carbonyl group. The "*l*-diene" and its oxidation products are therefore represented by the following partial formulæ :



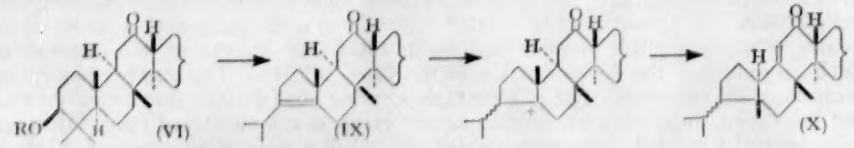
The position of the carbonyl group in the αβ-unsaturated ketone, and consequently in the βγ-unsaturated ketone, was disclosed by an examination of 12-oxoursan-3β-yl acetate (VI; R = Ac) and its relatives. When treated with hydriodic–acetic acid the oxo-acetate (VI; R = Ac) is converted into an αβ-unsaturated ketone, $C_{30}H_{48}O$, identical with that obtained as described above from the "*l*-diene." The αβ-unsaturated ketone is also obtained by the same treatment of either 12-oxo-13α-ursan-3β-yl acetate (VII) (Allan, Spring, and Stevenson, *J.*, 1955, 3072) or the enol acetate (VIII).



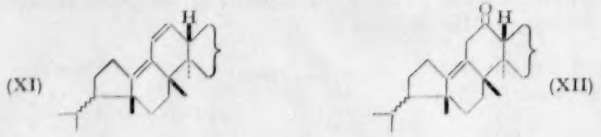
The acid-induced isomerisation of 5 : 8 : 14-trimethylnovursa-9(10) : 12-diene (IV) to the "*l*-diene" together with the established relation between the latter and the αβ-unsaturated ketone, $C_{30}H_{48}O$, show that the initial stages of the conversion of 12-oxoursan-3β-yl acetate (VI; R = Ac) into the αβ-unsaturated ketone include A-ring contraction and movement of a methyl group from $C_{(10)}$ to $C_{(5)}$, whereafter a double bond becomes conjugated with the 12-carbonyl group. A simple representation of this reaction includes the intermediate formation of 8 : 10 : 14-trimethylnovurs-3(5)-en-12-one (IX). Approach of a proton to the double bond of (IX) with synchronous (*a*) movement of the $C_{(10)}$-methyl group (β) to $C_{(5)}$, (*b*) movement of the 9-hydrogen (α) to $C_{(10)}$, and (*c*) loss of a proton from $C_{(11)}$ then leads to the αβ-unsaturated ketone (X).* If this reaction mechanism is correct, the "*l*-diene" will be (XI), and the βγ-unsaturated ketone will be (XII). Several

* An attractive reaction path is that in which the proton approaches from the rear (α) side, so affording a fully synchronous reaction. This would require that the *iso*propyl group in (X) is β-orientated; proof of the configuration of this group is however still lacking.

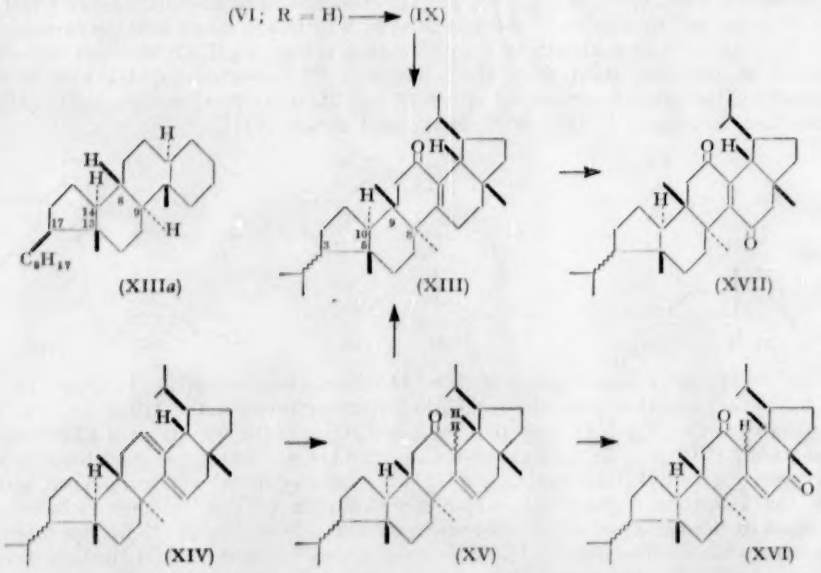
considerations, however, show that the three related formulæ (X), (XI), and (XII) cannot represent the αβ-unsaturated ketone, the "*l*-diene," and the βγ-unsaturated ketone respectively. First, the intensity of absorption in the ethylenic region of the spectrum



precludes the possibility that the double bond in the βγ-unsaturated ketone is exocyclic to two rings as in (XII). Secondly, the αβ-unsaturated ketone shows maximal absorption at 2600 Å, whereas by analogy with other 12-oxo-9(11)-enes, a compound of structure (X) should show maximal absorption at approximately 2500 Å. Finally, and more important,

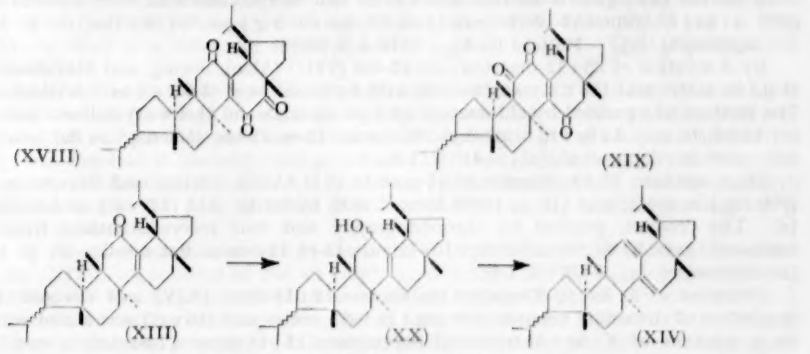


oxidation of the αβ-unsaturated ketone with chromic acid gives, in high yield, a bright yellow compound $C_{30}H_{46}O_2$ which shows the ultraviolet absorption of a fully transoid system. This behaviour proves that a methylene group is adjacent to the double bond in the αβ-unsaturated ketone.



The exclusion of (X) as the structure of the αβ-unsaturated ketone and the oxidation of this compound to a transoid ene-dione leads inevitably to the conclusion that the double bond in this compound is between $C_{(13)}$ and $C_{(14)}$. The formation of the αβ-unsaturated ketone from 12-oxoursan-3β-yl acetate (VI; R = Ac) must therefore include the movement of the methyl groups attached to $C_{(8)}$ and $C_{(14)}$. The reaction may be represented as

proceeding through 8 : 10 : 14-trimethylnovurs-3(5)-en-12-one (IX), with subsequent attack by a proton at the double bond in (IX) with synchronous (*a*) movement of the $C_{(10)}$-methyl group (β) to $C_{(5)}$, (*b*) movement of the 9-hydrogen (α) to $C_{(10)}$ (*c*) movement of the $C_{(8)}$-methyl group (β) to $C_{(9)}$, (*d*) movement of the $C_{(14)}$-methyl group (α) to $C_{(8)}$, and (*e*) loss of a proton from $C_{(13)}$. The αβ-unsaturated ketone is therefore 5 : 8α : 9β-trimethyl-10α-novurs-13-en-12-one (XIII). Accordingly the "*l*-diene" is 5 : 8α : 9β-trimethyl-10α-novursa-12 : 14-diene (XIV), the βγ-unsaturated ketone is 5 : 8α : 9β-trimethyl-10α-novurs-14-en-12-one (XV), the diketone $C_{30}H_{46}O_2$ is 5 : 8α : 9β-trimethyl-10α-novurs-14-ene-12 : 16-dione (XVI) and the transoid ene-dione is 5 : 8α : 9β-trimethyl-10α-novurs-13-ene-12 : 15-dione (XVII). The concerted reactions detailed above lead to a conformation in which the stereochemistry at positions 5, 10, 9, and 8 coincides with that at positions 13, 14, 8, and 9 in cholestane (XIII*a*) and we suggest that the urge to adopt this conform-



ation is at least part of the force causing the reaction (VI) ⟶ (XIII). As we shall show in a later paper an essential driving force is the *cis*-β-locking of rings D and E.

A mechanism similar to that described above is postulated for the conversion of α-amyrin (I) into the "*l*-diene" (XIV) by treatment with hydriodic acid, with the difference that final proton elimination occurs from $C_{(15)}$.

It is certain that the conversion of α-amyrin (I) into the "*l*-diene" (XIV) by shaking with phosphoric oxide in benzene at room temperature does not include the formation of either 8 : 10 : 14-trimethyl-5ξ-novursa-3(4) : 12-diene (III) or the 3(5) : 12-isomer (III*a*) as discrete intermediates since these two hydrocarbons are unchanged after the same treatment.* The reaction is probably *fully* concerted.

As stated above, oxidation of the αβ-unsaturated ketone (XIII) with chromic acid gives the ene-dione (XVII). More drastic oxidation of the αβ-unsaturated ketone, or of the ene-dione (XVII) with the same reagent, gives two isomeric compounds, $C_{30}H_{44}O_3$, which are considered to be 5 : 8α : 9β-trimethyl-10α-novurs-13-ene-12 : 15 : 16-trione (XVIII) and 5 : 8α : 9β-trimethyl-10α-novurs-13-ene-11 : 12 : 15-trione (XIX). The behaviour of the ene-dione (XVII) and of the two ene-triones on reduction will be reported later.

Reduction of 5 : 8α : 9β-trimethyl-10α-novurs-13-en-12-one (XIII) with lithium aluminium hydride gives a mixture of epimeric allylic alcohols (XX). Treatment of the mixture with either acetic anhydride and pyridine or hydrochloric–acetic acid gives 5 : 8α : 9β-trimethyl-10α-novursa-12 : 14-diene (XIV) identical with the "*l*-diene" obtained by dehydration of α-amyrin with phosphoric oxide.

Experimental

Rotations were measured in $CHCl_3$ and ultraviolet absorption spectra in EtOH solutions. Grade II alumina and light petroleum, b. p. 60—80°, were used for chromatography.

* These experiments were made by Mr. G. G. Allan to whom we express our best thanks.

5 : 8α : 9β-*Trimethyl*-10α-*novurs*-13-*ene*-12-*one* (XIII).—(*a*) A solution of 12-oxo-13α-ursan-3β-yl acetate (VII) (Allan, Spring, and Stevenson, *loc. cit.*) (2·0 g.) in glacial acetic acid (25 c.c.) was refluxed for 16 hr. with hydriodic acid (7 c.c.; *d* 1·7; freshly distilled from hypophosphorous acid). The mixture was diluted with water and extracted with ether, and the extract washed with sodium thiosulphate solution, and evaporated. The residue crystallised from aqueous methanol, to give 5 : 8α : 9β-*trimethyl*-10α-*novurs*-13-*en*-12-*one* as flat needles (400 mg.), m. p. 157—158·5°, $[\alpha]_D$ −41° (*c*, 1·6), $\lambda_{max.}$ 2600 Å (ε 9000) (Found : C, 84·9; H, 11·7. $C_{30}H_{48}O$ requires C, 84·8; H, 11·4%). It does not give a colour with tetranitromethane.

(*b*) A solution of 12-oxo-13α-ursan-3β-yl benzoate (Allan, Spring, and Stevenson, *loc. cit.*) (45 g.) in acetic acid (2 l.) was refluxed for 16 hr. with hydriodic acid (150 c.c.; *d* 1·7; freshly distilled from hypophosphorous acid). The mixture was concentrated, then diluted with water, and the product isolated as described above. A solution of the product in benzene–light petroleum (300 c.c.; 1 : 2) was chromatographed on alumina (1000 g.). Elution with the same solvent (4 l.) gave a fraction which after four recrystallisations from aqueous methanol gave 5 : 8α : 9β-trimethyl-10α-novurs-13-en-12-one (10·0 g.) as flat needles, m. p. 155—157° (no depression), $[\alpha]_D$ −38° (*c*, 1·0), $\lambda_{max.}$ 2610 Å (ε 8600).

(*c*) A solution of 3β : 12-diacetoxyurs-12-ene (VIII) (Allan, Spring, and Stevenson, *loc. cit.*) (1 g.) in acetic acid (15 c.c.) was treated with hydriodic acid (3·5 c.c.) as described under (*a*). The product was purified by chromatography on alumina and thrice crystallised from aqueous methanol, to give 5 : 8α : 9β-trimethyl-10α-novurs-13-en-12-one (550 mg.) as flat needles, m. p. 157—158° (no depression), $[\alpha]_D$ −41° (*c*, 1·8).

(*d*) A solution of 12-oxoursan-3β-yl acetate (VI) (Allan, Spring, and Stevenson, *loc. cit.*) (900 mg.) in acetic acid (18 c.c.) was treated with hydriodic acid (3·5 c.c.) as described under (*a*). The product, purified by chromatography and four recrystallisations from aqueous methanol, gave 5 : 8α : 9β-trimethyl-10α-novurs-13-en-12-one as flat needles, m. p. 158—159° (no depression), $[\alpha]_D$ −39° (*c*, 1·5).

Oxidation of 5 : 8α : 9β-*Trimethyl*-10α-*novursa*-12 : 14-*diene* (XIV) *with Chromic Acid.*—(*a*) A solution of chromium trioxide (540 mg.) in 90% acetic acid (15 c.c.) was added with stirring to a solution of 5 : 8α : 9β-trimethyl-10α-novursa-12 : 14-diene ("*l*-α-amyradiene"; Ewen *et al.*, *loc. cit.*) (2·0 g.) in benzene (20 c.c.) and glacial acetic acid (60 c.c.), and the mixture was kept at 100° for 1 hr. The product was isolated in the usual way and crystallised five times from chloroform–methanol, to give 5 : 8α : 9β-*trimethyl*-10α-*novurs*-14-*en*-12-*one* (XV) as needles (760 mg.), m. p. 218—219°, $[\alpha]_D$ −62° (*c*, 2·2), ε at 2050 Å = 3,500. Infrared absorption (in $CHCl_3$) : strong band at 1698 cm.$^{-1}$ (Found : C, 84·9; H, 11·4. $C_{30}H_{48}O$ requires C, 84·8; H, 11·4%). It gives a yellow colour with tetranitromethane. The ultraviolet spectrum showed the presence of *ca.* 5% of αβ-unsaturated ketone impurity, which could not be removed by crystallisation or chromatography.

(*b*) Chromium trioxide (3·0 g.) in acetic acid (150 c.c.) was added dropwise with stirring to a solution of 5 : 8α : 9β-trimethyl-10α-novursa-12 : 14-diene (3 g.) in glacial acetic acid (1·5 l.) at 100°. After being kept at 100° for 5½ hr. and overnight at room temperature, the mixture was worked up in the usual way. Crystallisation of the residue from chloroform–methanol yielded needles (900 mg.), m.p. 216—220°, $\lambda_{max.}$ 2500 Å (ε 7500), which were chromatographed in benzene–light petroleum (360 c.c.; 1 : 1) on alumina (100 g.). The product eluted with the same solvent (600 c.c.) crystallised from chloroform–methanol to give 5 : 8α : 9β-*trimethyl*-10α-*novurs*-14-*ene*-12 : 16-*dione* (XVI) as needles (320 mg.), m. p. 224—225°, $[\alpha]_D$ −134° (*c*, 1·2), $\lambda_{max.}$ 2500 Å (ε 10,500) (Found : C, 81·85; H, 10·4. $C_{30}H_{46}O_2$ requires C, 82·2; H, 10·5%). It does not give a colour with tetranitromethane.

Action of Alkali on 5 : 8α : 9β-*Trimethyl*-10α-*novurs*-14-*en*-12-*one* (XV).—The βγ-unsaturated ketone (250 mg.) in 5% methanolic sodium hydroxide (200 c.c.) was refluxed for 3 hr. Addition of water precipitated a solid which was recrystallised from aqueous methanol, to give 5 : 8α : 9β-trimethyl-10α-novurs-13-en-12-one (XIII) as needles, m. p. 155—157° (no depression), $[\alpha]_D$ −38° (*c*, 0·9), $\lambda_{max.}$ 2600 Å (ε 8600).

The βγ-unsaturated ketone (XV) was recovered unchanged by treatment with concentrated hydrochloric acid (1 part) in chloroform (2 parts) and acetic acid (5 parts) at 40° for 1 hr.

Oxidation of 5 : 8α : 9β-*Trimethyl*-10α-*novurs*-14-*en*-12-*one* (XV) *with Chromic Acid.*—Chromium trioxide (112 mg.) in acetic acid (5 c.c.) was added to a solution of the ketone (224 mg.) in benzene (3 c.c.) and acetic acid (1·8 c.c.), and the mixture heated at 100° for 1 hr. Crystallisation of the product, isolated in the usual way, from chloroform–methanol gave 5 : 8α : 9β-trimethyl-10α-novurs-14-ene-12 : 16-dione (XVI) as fine needles (93 mg.), m. p. 220—222° (no depression), $[\alpha]_D$ −130° (*c*, 0·8), $\lambda_{max.}$ 2500 Å (ε 10,100).

Oxidation of 5 : 8α : 9β-*Trimethyl*-10α-*novurs*-13-*en*-12-*one* (XIII) *with Chromic Acid.*—Chromium trioxide (4·8 g.) in 90% acetic acid (56 c.c.) was added to a solution of the ketone (8·0 g.) in acetic acid (580 c.c.), and the mixture stirred at 95° for 1 hr. The product, isolated by means of ether in the usual way, in benzene–light petroleum (3 : 7) was chromatographed on alumina. Elution with the same solvent (200 c.c.) gave a yellow solid (2·6 g.) which crystallised from methanol, to give 5 : 8α : 9β-*trimethyl*-10α-*novurs*-13-*ene*-12 : 15-*dione* (XVII) as flat yellow needles, m. p. 176—177°, $[\alpha]_D$ +86° (*c*, 2·7), $\lambda_{max.}$ 2260 and 2760 Å (ε 3400 and 8000) (Found: C, 82·1; H, 10·5. $C_{30}H_{46}O_2$ requires C, 82·1; H, 10·6%). Benzene–light petroleum (1 : 1; 500 c.c.) eluted an orange solid (0·84 g.) which on crystallisation from aqueous methanol yielded 5 : 8α : 9β-*trimethyl*-10α-*novurs*-13-*ene*-11(or 16) : 12 : 15-*trione* (XIX) or (XVIII) as long flat orange needles, m. p. 182—183°, $[\alpha]_D$ +214° (*c*, 1·8), $\lambda_{max.}$ 2220 and 2990 Å (ε 4600 and 5600) (Found: C, 79·4; H, 9·9. $C_{30}H_{44}O_3$ requires C, 79·6; H, 9·8%). Continued elution with the same solvent (200 c.c.) gave an orange solid (0·09 g.) which after six recrystallisations from aqueous methanol furnished 5 : 8α : 9β-*trimethyl*-10α-*novurs*-13-*ene*-12 : 15 : 16(or 11)-*trione* (XVIII) or (XIX) as yellow-orange needles, m. p. 228—230°, $[\alpha]_D$ +378° (*c*, 0·9), $\lambda_{max.}$ 2220 and 2960 Å (ε 3500 and 6000) (Found: C, 79·9; H, 10·1. $C_{30}H_{44}O_3$ requires C, 79·6; H, 9·8%).

Oxidation of 5 : 8α : 9β-*Trimethyl*-10α-*novurs*-13-*ene*-12 : 15-*dione* (XVII) *with Chromic Acid.*—Chromium trioxide (200 mg.) in acetic acid (5 c.c.) was added to the ene-dione (120 mg.) in acetic acid (20 c.c.) and the mixture stirred at 95° for 1 hr. The product, isolated in the usual way, was dissolved in benzene–light petroleum (1 : 1) and filtered through a short column of alumina. Crystallisation of the residue from aqueous methanol gave 5 : 8α : 9β-trimethyl-10α-novurs-13-ene-11(or 16) : 12 : 15-trione (XIX) or (XVIII) as flat needles (30 mg.), m. p. 178—180° (no depression).

5 : 8α : 9β-*Trimethyl*-10α-*novursa*-12 : 14-*diene* (XIV) *from* 5 : 8α : 9β-*Trimethyl*-10α-*novurs*-13-*en*-12-*one* (XIII).—A solution of the αβ-unsaturated ketone (1·0 g.) in dry ether (200 c.c.) was added dropwise to a suspension of lithium aluminium hydride (1·0 g.) in dry ether (200 c.c.), the mixture refluxed for 2 hr. and kept overnight at room temperature. The product, obtained by working up in the usual way, on crystallisation from chloroform–methanol yielded a mixture of the epimeric 5 : 8α : 9β-trimethyl-10α-novurs-13-en-12-ols (XX) as needles and prisms (0·68 g.) which gave a yellow colour with tetranitromethane and were not further purified. Concentrated hydrochloric acid (1 c.c.) was added to the mixture (100 mg.) in chloroform (2 c.c.) and acetic acid (20 c.c.), and the solution heated at 100° for 2 hr. On cooling, the solid which separated was collected and crystallised twice from chloroform–methanol, to yield 5 : 8α : 9β-trimethyl-10α-novursa-12 : 14-diene (80 mg.) as plates, m. p. 195—197° (no depression), $[\alpha]_D$ −112° (*c*, 2·6), $\lambda_{max.}$ 2340, 2410, and 2500 Å (ε 15,200, 16,400, and 10,000).

The mixture of alcohols (XX) (66 mg.) in pyridine (2 c.c.) and acetic anhydride (2 c.c.) was heated at 100° for 1 hr., worked up in the usual way, and the product crystallised several times from chloroform–methanol, to yield 5 : 8α : 9β-trimethyl-10α-novursa-12 : 14-diene (30 mg.), m. p. 194—196° (no depression), $[\alpha]_D$ −111° (*c*, 2·2), $\lambda_{max.}$ 2340, 2410, and 2500 Å (ε 13,300, 15,000, and 8,800).

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The Constitution and Synthesis of Leucoanthocyanidins.

By F. E. KING and J. W. CLARK-LEWIS.

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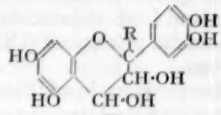
The catalytic reduction of 7 : 8 : 3′ : 4′-tetramethoxyflavonol gives a (±)-7 : 8 : 3′ : 4′-tetramethoxyflavan-3 : 4-diol to which a 2(e) : 3(a) : 4(e) conformation for the substituents at the 2 : 3 : 4-positions is attributed. It is further shown that the synthetic diol is the racemic modification of (−)-tetra-*O*-methylmelacacidin, thus completely identifying the phlobaphen–anthocyanidin-forming compound, melacacidin, a natural product probably typical in structure of the majority of leucoanthocyanidins.

LEUCOANTHOCYANIDINS are colourless phenolic substances which are converted into anthocyanidins by the action of aqueous or alcoholic acid, and the term leucoanthocyanin was introduced by Rosenheim (*Biochem. J.*, 1920, **14**, 178) to describe a supposedly glycosylated member of the series found in the young leaves and stems of the grape (*Vitis vinifera*). Investigations since Rosenheim's discovery of the first leucoanthocyan(id)in have been largely concerned with their distribution in the plant kingdom, and the extensive surveys of Robinson and Robinson (*Biochem. J.*, 1931, **25**, 1687; 1932, **26**, 1647; 1933, **27**, 206) have established their almost ubiquitous occurrence among the higher plants. Leucoanthocyanidins are invariably detected by converting them into the corresponding anthocyanidins, the products being identified either by means of colour reactions and partition methods (Robinson and Robinson, *loc. cit.*) or by the more recent paper-chromatographic technique (Bate-Smith, *J. Exp. Bot.*, 1953, **4**, 1; *Biochem. J.*, 1954, **58**, 122; Bate-Smith and Lerner, *ibid.*, p. 126). However, the formation of anthocyanidins from their leuco-compounds demands rather more vigorous conditions than are normally required for the regeneration of flavylium salts from the related carbinols; consequently, despite the evidently close relationship of the two series, the leucoanthocyanidins cannot be identical with the ordinary *pseudo*-bases. Robinson and Robinson (*loc. cit.*) accordingly proposed a structure for leucocyanidin, *i.e.*, (I; R = OH), which takes the form of a hydrated carbinol at the same oxidation state as that of the corresponding flavylium salt. A modified expression (I; R = H) was tentatively suggested by Bate-Smith (*J. Exp. Bot.*, 1953, **4**, 1), but no evidence was available with which to decide between the alternative formulæ.

The chemical investigation of leucoanthocyanidins is obstructed by difficulties arising from their amorphous character and from their occurrence as mixtures with other ill-defined substances of comparable physical properties. Moreover, the crude materials are slowly oxidised in the air and resemble the catechins (II) in their tendency to form intractable condensation polymers ("phlobaphens"). Definite indications as to the nature of leucoanthocyanidins were first obtained by King and Bottomley (*Chem. and Ind.*, 1953, 1368; *J.*, 1954, 1399) through the isolation from Australian blackwood (*Acacia melanoxylon*) of a new phenolic compound (melacacidin), $C_{15}H_{14}O_7$. Unlike the associated phenolic materials, melacacidin proved to be somewhat soluble in boiling ether and was therefore without difficulty extracted from the wood in a relatively pure condition. Although amorphous it readily formed crystalline derivatives, *e.g.*, a tetramethyl ether, which was identified as the flavandiol (III; R = Me). Apart from its uninvestigated prototype, flavan-3 : 4-diol (Mozingo and Adkins, *J. Amer. Chem. Soc.*, 1938, **60**, 669), no other flavan-3 : 4-diol was then known. The true character of melacacidin (III; R = H) was evident on treating it with boiling hydrochloric acid which afforded a deep cherry-red solution due to an anthocyanidin, shown by paper chromatography (King and Clark-Lewis, *Chem. and Ind.*, 1954, 757; see also Bottomley, *ibid.*, p. 516) to be 3 : 7 : 8 : 3′ : 4′-pentahydroxyflavylium chloride (IV) (Robinson and Vasey, *J.*, 1941, 660).

The structure of (−)-tetra-*O*-methylmelacacidin has since been confirmed by comparison of its properties with those of a synthetic (±)-7 : 8 : 3′ : 4′-tetramethoxyflavan-3 : 4-diol (III; R = Me) (King and Clark-Lewis, *loc. cit.*). The flavandiol was prepared by hydrogenation of 7 : 8 : 3′ : 4′-tetramethoxyflavonol (V) over Raney nickel, which

afforded a single crystalline racemate, m. p. 135—136° alone or mixed with the natural (−)-melacacidin tetramethyl ether, m. p. 146°. The identification of this racemate as (±)-tetra-*O*-methylmelacacidin, which was inherently probable from the m. p. observations, was confirmed by measurements of the infrared absorption, carbon tetrachloride solutions of the synthetic material and of (−)-melacacidin tetramethyl ether having coincident spectra. We are indebted to Dr. F. B. Strauss for these determinations and for his opinion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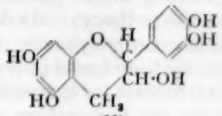
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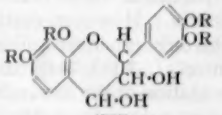
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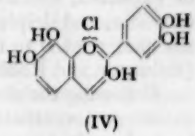
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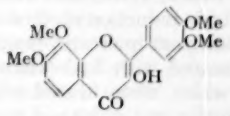
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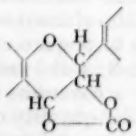
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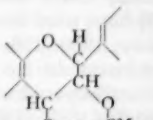
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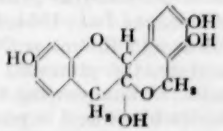
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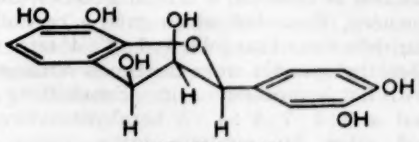
(VIII) Melacacidin

as to the relation of the two samples. The synthetic compound (III; R = Me) formed a diacetate, m. p. 157—158°, which had mixed m. p. 167—168° with the (−)-diacetate, m. p. 194°. A cyclic carbonate (VI), m. p. 205° (decomp.), was obtained by treating the (±)-diol with carbonyl chloride and triethylamine in toluene, and a mixture of this derivative with (−)-tetra-*O*-methylmelacacidin carbonate, m. p. 209° had m. p. 201—202° (decomp.). From the formation of a cyclic carbonate it may be assumed—as with the natural compound (King and Bottomley, *loc. cit.*)—that the synthetic diol also possesses the *cis*-configuration. This conclusion receives strong confirmation from the formation of an *iso*propylidene derivative (VII) of the racemic flavandiol since it is known that cyclic acetals are not normally obtained from *trans*-α-diols (" Progress in Stereochemistry," ed. W. Klyne, Butterworths, 1954, Vol. I, p. 55).

Since the catalytic reduction of ethylenic bonds invariably proceeds by *cis*-addition, it is possible to deduce the complete conformational structure of the flavandiol prepared by hydrogenation of 7 : 8 : 3′ : 4′-tetramethoxyflavonol (V) which accordingly results in a product wherein the 2-aryl and the 3-hydroxyl substituent are in the *cis*-configuration. The 3-hydroxyl group having already been shown to be a constituent of a *cis*-3 : 4-diol, it follows that all three substituents (aryl : hydroxyl : hydroxyl) at the adjacent asymmetric centres are *cis*-related, and in view of the spectroscopic evidence already quoted this must also be true of the tetra-*O*-methylmelacacidin and therefore of melacacidin.

Two principal conformations, 2(a) : 3(e) : 4(a) and 2(e) : 3(a) : 4(e), are thus possible for the natural flavandiol (III; R = H) and its compounds, which in their stereochemistry present a problem similar to that discussed in connexion with the catechins (King, Clark-Lewis, and Forbes, *J.*, 1955, 2948). Of the alternatives, the 2(e) : 3(a) : 3(e) disposition (VIII) is intrinsically the more probable since both the largest substituent, *i.e.*, the dihydroxyphenyl, and the numerically larger number of groups other than hydrogen are equatorially situated. In this energetically favoured arrangement the 4-hydroxyl group has the equatorial conformation which is, in fact, the configuration normally resulting from the slow catalytic reduction of an unhindered carbonyl group (*op. cit.*, p. 74). The generation of a 2 : 3-*cis*-derivative by reduction of the tetramethoxyflavonol (V) is analogous to

the formation of (±)-penta-*O*-methyl*epi*catechin in preference to the catechin ether by hydrogenation of 3 : 5 : 7 : 3′ : 4′-penta-*O*-methylquercetin (Freudenberg and Kammüller, *Annalen*, 1927, **451**, 209).

Melacacidin is so far the only fully characterised flavandiol to have been isolated from natural sources, but in view of the wide distribution of ill-defined phenolic substances which share its anthocyanidin-forming properties, the discovery of analogues can doubtless be expected, and in particular those corresponding to the principal species pelargonidin, cyanidin, and delphinidin. However, neither the anthocyanidin derived from melacacidin nor that related to the only other recognised leucoanthocyanidin, namely, peltogynol (IX) (Robinson and Robinson, *J.*, 1935, **744**), has so far been found in Nature.

Following the elucidation of the flavandiol structure for leucoanthocyanidins, in addition to our own synthetic experiments, methods for the preparation of flavan-3 : 4-diols have been described in preliminary notes from other laboratories. Bauer, Birch, and Hillis (*Chem. and Ind.*, 1954, 433) have used the lithium aluminium hydride reduction method of Mirza and Robinson (*Nature*, 1950, **166**, 997) to prepare cyanidin from quercetin penta-acetate, the presumed intermediate flav-2-en-3 : 4-diol being treated with hydrochloric acid. Accompanying the anthocyanidin was a colourless gum which when heated with hydrochloric acid in propan-2-ol yielded a further quantity of cyanidin and which was thus assumed to be the flavan-3 : 4-diol. Swain (*Chem. and Ind.*, 1954, 1144) has reported the sodium borohydride reduction of taxifolin, a natural 2 : 3-dihydroquercetin, to an amorphous, possibly stereoisomeric, flavandiol which gave a crystalline tetramethyl ether, also formed by the similar reduction of taxifolin 5 : 7 : 3′ : 4′-tetramethyl ether. Cyanidin and 5 : 7 : 3′ : 4′-tetra-*O*-methylcyanidin were thereupon obtained by treatment of the respective flavandiols with hot hydrochloric acid. Freudenberg and Roux (*Naturwiss.*, 1954, **41**, 450) prepared a 3 : 4 : 7 : 3′ : 4′ : 5′-hexahydroxyflavan and its crystalline 7 : 3′ : 4′ : 5′-tetramethyl ether by catalytic hydrogenation of natural dihydrorobinetin and subsequent methylation, and state briefly that 3 : 4 : 5 : 7 : 3′ : 4′-hexahydroxyflavan may be similarly obtained from dihydroquercetin. Lithium aluminium hydride was used for the preparation of 4′-methoxy-6-methylflavan-3 : 4-diol (Joshi and Kulkarni, *Chem. and Ind.*, 1954, 1421), and two racemates of the melacacidin structure (III; R = Me), m. p. 131—132° and 179°, have been obtained by catalytic and lithium aluminium hydride reduction, respectively, of synthetic 7 : 8 : 3′ : 4′-tetramethoxydihydroflavonol (Kulkarni and Joshi, *ibid.*, p. 1456).

The employment of dihydroflavonols for the preparation of flavandiols suffers from the disadvantage that they are not readily available by synthesis, and only a limited number of the naturally occurring compounds are known. Moreover, the stereochemistry of the existing dihydroflavonols has not yet been investigated, and consequently the configuration of the resulting flavandiols, which contain three centres of asymmetry and can therefore theoretically exist in four pairs of enantiomers, will be entirely unknown. Mahesh and Seshadri (*Proc. Indian Acad. Sci.*, 1955, **41**, 210) have recently discussed the stereochemistry of 3-hydroxyflavanones.

Kulkarni and Joshi (*loc. cit.*) postulate a 2(e) : 3(e)-arrangement for the aryl and the hydroxyl group in the dihydroflavonol used in their experiments, and a 2(e) : 3(e) : 4(e)-configuration (diol system *trans*) for its lithium aluminium hydride reduction product, m. p. 179° (diacetate, m. p. 122—123°). The product, m. p. 131—132° (diacetate, m. p. 120°), obtained by catalytic hydrogenation is regarded as the 2(e) : 3(e) : 4(a)-isomer, but no experimental evidence has been adduced in support of the *cis*-configuration thus attributed to the diol grouping. Clearly, the higher-melting diol is not (±)-tetra-*O*-methylmelacacidin, and the possible correspondence between the isomer of m. p. 131—132° and our synthetic diol of m. p. 135—136° is not confirmed by a comparison of the respective acetates of m. p. 120° and 157—158°. Moreover, we have been able to verify the non-identity of these products by mixed m. p. determinations with specimens kindly provided by Dr. Kulkarni. It is apparent therefore that three of the four theoretically possible racemates of structure (III; R = Me) are now known, the compound which is the principal subject of this communication being (±)-tetra-*O*-methylmelacacidin.

The transformation of melacacidin into the corresponding anthocyanidin is an oxidation

and it may therefore occur either through the intervention of atmospheric oxygen or by a disproportionation in which an equivalent of the flavandiol is reduced to a lower oxidation state. Rosenheim (*loc. cit.*) and Robinson and Robinson (*Biochem. J.*, **1933**, **27**, 206) have shown that air is not essential for the conversion of leucoanthocyanidins into flavylium salts, and assuming that the compounds which were the subject of their observation consisted of flavandiols, this can be construed as support for the disproportionation hypothesis. A possible mechanism leading to the simultaneous formation of a flavan-3-ol (catechin type) has already been propounded (King and Bottomley, *locc. cit.*) and it is significant that catechins have been detected by paper chromatography among the products from the action of acid on cacao " leucocyanidin " (Forsyth, *Nature*, 1953, **172**, 726).

The quantity of anthocyanidin formed in the acid treatment of melacacidin is small and is estimated as approximately 10%. This is in agreement with observations made with crude natural tannins (Bate-Smith and Swain, *Chem. and Ind.*, **1953**, **377**) which in view of their general similarity to melacacidin can now be regarded as leucoanthocyanidins. The low yield of flavylium salt is due to a competing reaction leading to " phlobaphen," an acid-catalysed polymerisation characteristic of the catechins (flavan-3-ols) and presumably, therefore, also of the analogous flavan-3 : 4-diols. Freudenberg and Weinges have in fact recently demonstrated (*Annalen*, 1954, **590**, 140) that the sensitivity of the flavans towards acid is unaffected by the degree of hydroxylation of the heterocyclic nucleus, and the tendency to condensation is furthermore greatest with those containing hydroxyl substituents at the 7- and the 4′-position, as in melacacidin. However, anthocyanidins have not been detected among the products of acid treatment of the catechins (Bate-Smith and Swain, *loc. cit.*), the 3 : 4-diol grouping therefore being essential to flavylium salt formation (cf. Freudenberg and Weinges, *loc. cit.*).

Experimental

(±)-*Melacacidin Tetramethyl Ether* (7 : 8 : 3′ : 4′-*Tetramethoxyflavan*-cis-3 : 4-*diol*) (III; R = Me).—Tetramethoxyflavonol (50—70%), m. p. 222°, was obtained from 2-hydroxy-3 : 4 : 3′ : 4′-tetramethoxychalkone, m. p. 126—127° (Crabtree and Robinson, *J.*, 1922, **121**, 1033) by treatment with alkaline peroxide (King and Bottomley, *J.*, 1954, **1399**; cf. Kostanecki and Rudse, *Ber.*, 1905, **38**, 935). The 3-*ethoxycarbonyl* derivative (90%) was formed from ethyl chloroformate and crystallised from ethanol in yellow needles, m. p. 143—144° (Found : C, 59·5; H, 5·4; loss, 4·3. $C_{22}H_{22}O_9,H_2O$ requires C, 58·9; H, 5·4; loss, 4·0. Found, in a specimen dried at 110° *in vacuo* : C, 61·9; H, 5·4. $C_{22}H_{22}O_9$ requires C, 61·4; H, 5·2%).

7 : 8 : 3′ : 4′-Tetramethoxyflavonol (2 g.) in ethanol (100 c.c.) was hydrogenated for 16 hr. at 100—110°/100 atm. over Raney nickel (*ca.* 4·0 g.). After filtration from catalyst (kieselguhr) the solvent was removed under reduced pressure, and a solution of the residue in benzene (30—40 c.c.) was cautiously diluted with light petroleum (b. p. 40—60°; *ca.* 25 c.c.). Next day, 7 : 8 : 3′ : 4′-*tetramethoxyflavan*-cis-3 : 4-*diol* [(±)-*melacacidin tetramethyl ether*] (0·8 g., 40%), m. p. 131—132°, was collected (Found : C, 62·7; H, 6·4. $C_{19}H_{22}O_7$ requires C, 63·0; H, 6·1%). Recrystallisation from benzene–light petroleum afforded the (±)-diol in prisms, m. p. 135—136° alone and when mixed with (−)-melacacidin tetramethyl ether (needles, m. p. 146°). Light absorption of (±)- and (−)-melacacidin tetramethyl ether in ethanol : $\lambda_{max.}$ 206 (ε 69,400) and 278 mμ (ε 3850). Acetylation of the diol (0·1 g.) with acetic anhydride–pyridine at room temperature overnight afforded the (±)-*diacetate*, needles or small prisms, m. p. 157—158°, from methanol (Found : C, 61·7; H, 5·5; Ac, 21·3. $C_{23}H_{26}O_9$ requires C, 61·9; H, 5·9; Ac, 19·3%). A mixture of the (±)-diacetate with (−)-melacacidin tetramethyl ether diacetate (needles, m. p. 194°; King and Bottomley, *loc. cit.*) melted at 167—168°. The preparation of the (±)-diol was repeated several times, the best results being obtained with small quantities of the flavonol (2—4 g.) and relatively large amounts of catalyst.

The infrared absorption spectra of (±)- and (−)-melacacidin tetramethyl ether were measured in CCl_4 solutions 1 mm. thick, with solvent compensation by double-beam operation. The positions of maxima and minima for each compound coincided exactly throughout the range 2—11·5 μ, although owing to the thickness of solutions (1 mm.), which was necessitated by sparing solubility, the regions of intense solvent absorption (6·2—6·7 and 7·8—8·4 μ) are without significance.

A mixture of the *cis*-diol, m. p. 132° (Kulkarni and Joshi, *Chem. and Ind.*, 1954, 1456) with

(±)-melacacidin tetramethyl ether (m. p. 135—136°) sintered at 111° and melted at 116° to a turbid liquid which cleared at 126°; a similar mixture with (−)-melacacidin tetramethyl ether (m. p. 145—146°) melted at 115—117°. A mixture of the *cis*-diol diacetate (m. p. 120°) (Kulkarni and Joshi, *loc. cit.*) with (±)-melacacidin tetramethyl ether diacetate (m. p. 156—157°) sintered at 109° and melted at 113—115°. We thank Dr. Kulkarni for the provision of the relevant specimens for these mixed m. p. determinations.

(±)-7 : 8 : 3′ : 4′-*Tetra*-O-*methylmelacacidin* 3 : 4-*Carbonate* (VI).—(*a*) A solution of the *cis*-(±)-diol (0·3 g.) in benzene (*ca.* 5 c.c.) was treated dropwise with a solution of carbonyl chloride in toluene (12·5% w/w, 0·75 c.c., 1 equiv.) at room temperature. After 1 hr. triethylamine (1 c.c., *ca.* 9 equiv.) was added and the solution cooled in water during the dropwise addition of further carbonyl chloride solution (2·25 c.c., total 3·0 c.c., 4 equiv.); the mixture was then left at room temperature for 2 hr. before the addition of water and ether. Filtration afforded (±)-7 : 8 : 3′ : 4′-*tetra*-O-*methylmelacacidin carbonate* (0·22 g., 69%), m. p. 205° (decomp.), which crystallised from ethanol (50 c.c.) in aggregates of platelets (0·138 g.), m. p. 205° (decomp.) (Found: C, 61·8; H, 5·2. $C_{20}H_{20}O_8$ requires C, 61·8; H, 5·2%). A mixture of the (±)-carbonate with (−)-melacacidin tetramethyl ether carbonate [needles, m. p. 209° (decomp.)] (King and Bottomley, *loc. cit.*) melted at 201—202° (decomp.). In common with other acyl derivatives of melacacidin tetramethyl ether the carbonate became pale pink when dried in a vacuum-desiccator over sulphuric acid. It was insoluble in exaltone and camphor except at temperatures (180—200°) causing decomposition with evolution of gas.

(*b*) Attempts to prepare the carbonate by the action of ethyl chloroformate on the diol in aqueous alkali (King and Bottomley, *loc. cit.*) failed, but were successful in benzene. Addition of triethylamine (1·0 c.c.) to the diol (0·1 g.) and ethyl chloroformate (1·0 c.c.) in benzene (5 c.c.) containing a little dioxan, caused the solution to boil, and after 2 hr. at room temperature the mixture was filtered and the residue washed with water. Crystallisation of the residue from ethanol (15 c.c.) afforded the carbonate (0·0314 g., 30%), plates, m. p. 204—205° (decomp.), identical with that described under (*a*), and a further 20% (total 50%) was obtained by crystallisation of the residue from evaporation of the benzene solution. The possibility that the formation of the carbonate under these conditions is due to carbonyl chloride present in the ethyl chloroformate was not investigated.

iso*Propylidene Derivative of* (±)-7 : 8 : 3′ : 4′-*Tetramethylmelacacidin* (VII).—(±)-Melacacidin tetramethyl ether (0·093 g.) was dissolved in acetone (6 c.c.) containing hydrochloric acid (1 drop in 100 c.c.), and after 3 days at room temperature triethylamine (2 drops) and water were added to the clear solution. Crystallisation afforded the iso*propylidene derivative* in large elongated leaflets (0·082 g., 80%), m. p. 163°, which crystallised from methanol with almost quantitative recovery in prisms, m. p. 163° (Found: C, 65·6; H, 6·6. $C_{22}H_{26}O_7$ requires C, 65·7; H, 6·5%).

Anthocyanidin Formation.—(±)- and (−)-Melacacidin tetramethyl ether were unaffected by acid in the cold for short periods, but both the synthetic and the natural flavan-3 : 4-diol gave an intense cherry-red colour with hydrochloric acid (10%) in butanol at 100°. On paper chromatograms the two coloured solutions behaved characteristically and identically: with ascending butanol–2N-hydrochloric acid there were observed red spots (attributed to 3-hydroxy-7 : 8 : 3′ : 4′-tetramethoxyflavylium chloride) at R_F 0·94, with a brownish-yellow tail (R_F *ca.* 0·84) due to "phlobaphen," and a further colourless tail (extending to R_F 0·57) which showed a bright greenish-yellow fluorescence in ultraviolet light. In ascending *m*-cresol–2N-hydrochloric acid the flavylium salts moved with the solvent front and these red spots were edged with the brownish-yellow material and by a narrow region which fluoresced in ultraviolet light. (−)- and (±)-Melacacidin tetramethyl ether moved as single substances on paper chromatograms and the colourless spots were revealed by spraying the developed chromatograms with concentrated hydrochloric acid and heating at 100° for 2—3 min., which caused the appearance of the red colour due to 3-hydroxy-7 : 8 : 3′ : 4′-tetramethoxyflavylium chloride. The two materials behaved identically and showed R_F 0·86 in butanol–acetic acid–water (5 : 1 : 4) and R_F 0·96—1·0 in *m*-cresol–acetic acid–water (50 : 2 : 48).

7 : 8 : 3′ : 4′-Tetramethoxyflavanone (40%), m. p. 143—144°, was prepared as described by Geissman and Heaton (*J. Amer. Chem. Soc.*, 1944, **66**, 486—487) except that fractional crystallisation was avoided and isolation simplified by extraction of the concentrated reaction mixture with ether, removal of phenolic material by washing with 0·5N-sodium hydroxide, and evaporation of the ether to yield the crystalline flavanone.

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Infrared Spectra of Semicarbazones.

By W. H. T. Davison and (Miss) P. E. Christie.

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The infrared spectra of twenty-four semicarbazones of common ketones and aldehydes are reported. The semicarbazones are very suitable for spectroscopic identification in addition to being easier to isolate than liquid ketones.

The semicarbazone grouping gives characteristic absorptions at about **3460**, **3370—2800**, and **767** cm.$^{-1}$ which are assigned to NH stretching and rocking modes. Strong absorptions at **1695** and **1585** cm.$^{-1}$ are assigned to the amide I and II bands; a rather variable absorption at **1665** cm.$^{-1}$ is very tentatively assigned to a C=N stretching mode.

Although the identification of ketones by their direct infrared spectra is usually possible, they are, when liquids, relatively difficult to isolate and purify on a small scale. Thus identification is often made by way of a 2 : 4-dinitrophenylhydrazone or a semicarbazone. Spectra of the former have been reported (Ross, *Analyt. Chem.*, 1953, **25**, 1288) but not of the latter. The semicarbazones however have better crystalline character and more distinctive melting points, and are more suitable for elemental analysis.

It was to be expected that the spectra of the semicarbazones would be more readily differentiated than those of the 2 : 4-dinitrophenylhydrazones, which are dominated by the $C_6H_3(NO_2)_2$·NH·N:C group (*idem*, *loc. cit.*).

Experimental.—The semicarbazones were prepared on a 0·5-g. scale by standard methods (Hickinbottom, " Reactions of Organic Compounds," Longmans, Green and Co., London, 1948, p. 162) and were recrystallised, usually from alcohol, until they gave satisfactory m. p.s.

Samples were originally examined as perfluorocarbon mulls in the **3500—2500** cm.$^{-1}$ region, by use of a lithium fluoride prism, and as paraffin mulls in the sodium chloride region. Thicknesses are not therefore comparable for the two regions. Later measurements were made with pressed potassium chloride discs (Schiedt, *Naturforsch.*, 1952, **76**, 270; Stimson, *J. Amer. Chem. Soc.*, 1952, **74**, 1805). Spectra of paraffin mulls have a break in the region of strong paraffin absorptions at **1450** and **1375** cm.$^{-1}$.

The Table lists m. p.s and the frequencies and intensities of the main characteristic absorption.

Results and Discussion.—The spectra show clear sharp bands (see Figure) and are eminently suitable for the identification of ketones or aldehydes. It is not possible to differentiate ketones from aldehydes as a class; this was also observed for the 2 : 4-dinitrophenylhydrazones (Ross, *loc. cit.*). The semicarbazones appear to be more readily differentiated from one another than are the 2 : 4-dinitrophenylhydrazones, as had been expected.

In some cases attempts were made to form polymorphs by crystallisation from different solvents and from melts; no evidence of polymorphism was observed. However, both geometrical isomerism and polymorphism may occur in these derivatives (Kon and Nutland, *J.*, 1926, 3101.). If, however, the semicarbazones are recrystallised under the same conditions, the spectra should be satisfactory for identification, even where polymorphic modifications can occur and give rise to different spectra (Kendall, *Analyt. Chem.*, 1953, **25**, 382.).

From the structure of the semicarbazones, RR'·C:N·NH·CO·NH_2, a number of characteristic vibrational modes would be expected, *e.g.*, ν(NH), ν(C:O), δ(NH), and ν(C:N). Of these, all but the ν(C:N) are common to amides, which are known (Bellamy, " Infrared Spectra of Complex Molecules," Methuen, London, 1954, p. 175) to give rise to ν(NH), an " amide I " band [ν(C:O)] at about **1650** and " amide II " band at about **1600** cm.$^{-1}$. There has been much controversy (Bellamy, *op. cit.*, p. 185) as to whether the " amide II " band is mainly δ(NH) or ν(C–N).

Semicarbazone of :	M. p.	C.S. No.*	ν(NH) unbonded	ν(NH) bonded	Amide I	ν(C:N)	Amide II	δ(NH) unbonded
(Semicarbazide hydrochloride)	—	251	3440(6)	3318(5), 3254(7), 3065(5), 2880(8b)	1695(7)	—	1590(6)	772(3)
Acetone	190—191° †	252	—	3322(4), 3248(4), 3175(4), 3070(2)	1690(6)	1650(2), 1624(3)	1556 (6)	—
Ethyl methyl ketone	137	253	3460(7)	3342(6), 3179(9b)	1695(9)	1667(7)	1588(9)	767(3)
Diethyl ketone	139	254	3470(7)	3348(3), 3190(6b)	1700(8)	1665(3)	1592(7)	766(2)
Methyl *n*-propyl ketone	106	255	3434(3)	3357(2), 3299(3), 3202(5)	1688(7)	1663(sh), 1638(sh)	1595(6)	770(1)
Methyl *iso*propyl ketone	131	256	3475(6)	3359(sh), 3211(7b)	1713(9), 1698(sh)	1662(5)	1593(9)	765(3)
*iso*Butyl methyl ketone	131	257	3465(3)	3344(sh), 3278(sh), 3206(6)	1688(9)	—	1603(8)	774(1)
tert.-Butyl methyl ketone	156	258	3490(9)	3371(2), 3278(sh), 3208(9), 3165(sh)	1720(9)	1646(3)	1593(9)	763(4)
Di*iso*propyl ketone	159—160	259	3454(3)	3360(sh), 3335(3), 3204(3), 3099(2)	1695(6)	1665(7)	1565(4)	764(2)
Di*iso*butyl ketone	122	260	3485(4)	3346(sh), 3260(sh), 3194(5b), 3156(sh)	1700(8)	1675(7)	1577(6)	771(2)
Acetonylacetone	220	261	3461(6)	3334(3), 3184(5b)	1695(9)	1665(sh)	1590(8)	765(3)
*cyclo*Hexanone	167	262	3465(6)	3335(sh), 3258(5), 3196(5), 3141(sh)	1697(9)	1675(sh)	1580(7)	767(3)
3-Methyl*cyclo*hexanone.....	191—192	263	3470(4)	3344(1), 3242(4), 3120(4)	1700(9)	1680(sh), 1655(sh)	1584(4)	768(2)
3 : 3 : 5-Trimethyl*cyclo*hexanone ...	190	264	3432(4)	3326(5), 3210(6), 3109(4), 3040(3)	1695(8)	1665(9), 1610(5)	1568(7)	763(2)
Acetaldehyde	165	265	3443(6)	3330(5), 3204(6), 3085(4)	1726(5)	1680(7), 1648(5)	1605(6)	764(1)
Heptanal	106	266	3438(3)	3297(3), 3192(3b), 3076(2)	1685(5)	1650(6)	1625(7)	767(2)
Cinnemaldehyde	211—212	267	3465(4)	3285(3), 3170(3b), 3059(2), 1722(5)	1722(5)	1675(5), 1650(5)	1605(5)	NA
Methyl *iso*propenyl ketone	173	268	3467(9)	3356(2), 3270(7), 3184(9), 3150(8), 3092(7)	1720(9)	1665(sh), 1620(sh)	1594(9)	763(5)
Acetophenone	200	269	3485(4)	3364(1), 3280(2), 3138(5b)	1750(9)	—	1590(9)	772(?)
m-Nitroacetophenone	>220	270	3470(7)	3360(2), 3278(3), 3192(6b), 3158(sh)	1725(9)	1622(2)	1593(7)	NA
Benzophenone	165—166	271	3478(5)	3352(4), 3285(4), 3200(5b), 3126(sh.b)	1705(9)	—	1587(6)	NA
Benzaldehyde	214	272	3453(3)	3286(4), 3180(4), 3068(4)	1700(6)	1660(7)	1607(8)	NA
o-Nitrobenzaldehyde	244	273	3468(3)	3368(1), 3291(2), 3230(2), 3175(3)	1745(5)	1675(1)	1607(4)	NA
p-Dimethylaminobenzaldehyde	216 †	274	3468(3)	3290(3), 3180(3b)	1691(6)	1650(6)	1610(8)	NA
2 : 3-Dimethoxybenzaldehyde	229 †	275	3442(3)	3283(2), 3165(3b)	1697(8)	—	1593(6)	NA
2-Hydroxy-3-methoxybenzaldehyde	221—222 †	276	3442(3)	3274(2), 3161(5b)	1674(7)	—	1600(6)	NA

* Spectra have been deposited with Chemical Society. Photocopies may be obtained, price 3*s.* 0*d.* per copy per spectrum, on application, quoting the C.S. No., to the General Secretary, The Chemical Society, Burlington House, Piccadilly, London, W.1.

† With decomp. b = broad; sh = shoulder; intensities (in tenths absorption) in parentheses; NA = not assigned.

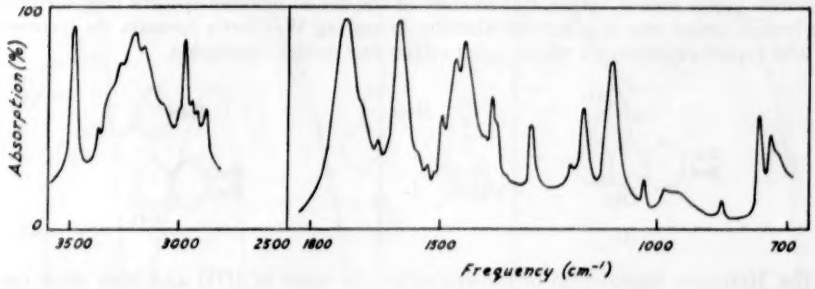
The aliphatic ketone semicarbazones show the following characteristic bands (cm.$^{-1}$), which are tentatively assigned as follows :

3460 ± 16 (sharp)	Unbonded $\nu_a(NH_2)$ or ν(NH)
3370 — 2800	Bonded ν(NH) and/or unbonded $\nu_a(NH_2)$
1695 ± 5	" Amide I " — ν(C:O)
ca. 1665	ν(C:N)
1585 ± 10	" Amide II "
767 ± 4	δ(NH) rocking (unbonded)

It is notable that, except for the 1665-cm.$^{-1}$ band, all the characteristic absorptions of semicarbazones are also shown by semicarbazide hydrochloride.

The 1665-cm.$^{-1}$ band is extremely variable, ranging from the strongest in this region (acetaldehyde, *iso*phorone, di*iso*propylsemicarbazones) to very weak bands or shoulders in some cases; it is entirely absent in semicarbazide hydrochloride. ν(C:N) occurs at 1640—1690 cm.$^{-1}$ (Bellamy, *op. cit.*, p. 226) and its intensity varies widely; we therefore tentatively assign the 1665-cm.$^{-1}$ absorptions to this mode.

Infrared spectrum of tert.*-butyl methyl ketone semicarbazone (crystalline in a potassium chloride pressed disc).*



Most of the semicarbazones have absorptions in the 1100-cm.$^{-1}$ region which are probably due to ν(CN).

In addition to a sharp band at about 3460 cm.$^{-1}$ [unbonded ν(NH)] there is a complex series of bands between 3370 and 3000 cm.$^{-1}$ which is similar to the broad ν(OH) absorption of carboxylic acids and is assigned to bonded ν(NH) modes. In most cases (*e.g.*, *tert.*-butyl methyl ketone semicarbazone, see Figure) a broad band extends over about 300 cm.$^{-1}$ with only slight evidence of complexity; in other cases (*e.g.*, di*iso*propyl ketone semicarbazone) a number of well-resolved absorptions are observed.

The complexity of the spectra in this region and that of the CH stretching modes is sufficient to permit the identification of semicarbazones in the 3500—2500 cm.$^{-1}$ region by using a relatively inexpensive near-infrared spectrometer.

Acetone semicarbazone (C.S. No. 252) is anomalous in showing no unbonded ν(NH) and no 767-cm.$^{-1}$ band. We therefore tentatively assign the 767-cm.$^{-1}$ band to a rocking mode of an *unbonded* NH. Its diagnostic value is somewhat reduced by other absorptions in this region in aromatic derivatives.

The marked shifts of ν(C:O) in the aromatic derivatives merit further study, by means of a series of substituted benzaldehydes and acetophenone derivatives; the shifts should be related to Hammett's σ function.

We thank Dr. G. B. Barlow for preparing some of the semicarbazones and Mr. G. R. Bates for measuring some of the spectra. We are grateful to the Dunlop Rubber Company for permission to publish this work which was carried out while one of us (P. E. C.) was employed as a vacation student.

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Lycoris *Alkaloids. Part XXXI.* A Structural Inter-relationship of Lycorine and Lycorenine.*

By Shojiro Uyeo and Haruaki Yajima.

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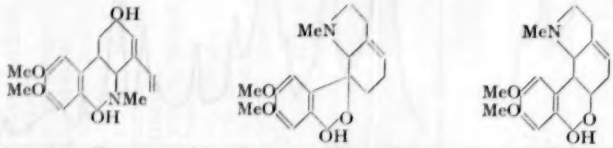
The Wolff–Kishner reduction of lycorenine (III) gave the dihydrodeoxy-compound (VI) which was converted by dehydrogenation into an indole (VII) identical with the compound derived from the Emde base (X) of lycorine by demethylenation followed by methylation and dehydrogenation.

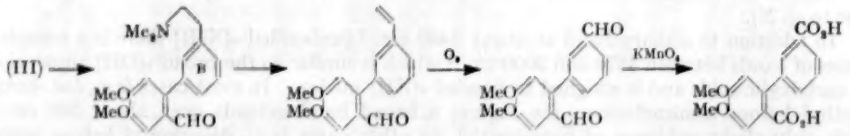
The structure of lycorenine advanced previously has thus been confirmed.

On the basis of theoretical discussions the formula (I) assigned by Kondo and Ikeda (*Ann. Rep. Itsuu Lab.*, 1952, **3**, 55) to lycorenine was recently changed by Wenkert and Hansen (*Chem. and Ind.*, 1954, 1262) to the semiacetal structure (II). However, as has been pointed out by us, lycorenine can be oxidized to homolycorine which is a δ-lactone, and this and other evidence leads to the revised formula (III) (Part XXIX *). Boit, Paul, and Stender (*Chem. Ber.*, 1955, **88**, 133) have independently shown that oxidation of lycorenine yields homolycorine, but in spite of the use of infrared spectra they considered that homolycorine was a γ-lactone, thereby favouring Wenkert's formula for lycorenine. We now report experiments which substantiate our earlier conclusion.

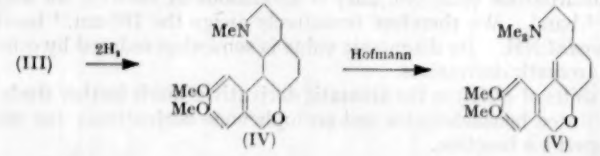


(I) (II) (III)

The Hofmann degradation of lycorenine on the basis of (III) and later steps can be readily interpreted as follows :



This degradation, however, does not fix the point of attachment of the nitrogen atom to ring B, but this could be inferred from the fact that the ultraviolet absorption spectrum of the methine (V) formed from dihydro-α-deoxylycorenine (IV), originally called "*d*-desoxydihydro-R-lycorenine," shows a double bond conjugated to the aromatic nucleus.



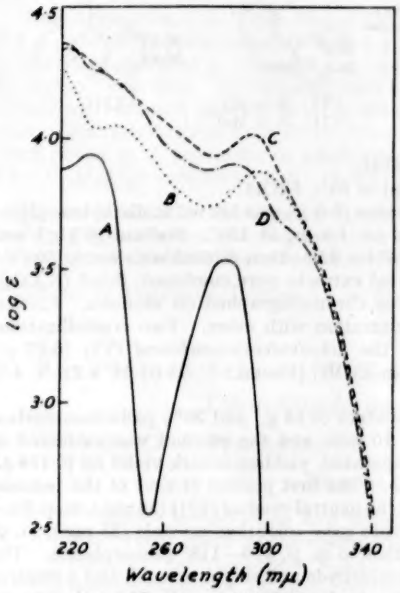
(IV) (V)

Conclusive proof that the nitrogen occupies the position shown in (III), and that the potential hydroxyl group must be secondary and not tertiary is provided by the following experiments. Wolff–Kishner reduction of lycorenine afforded the dihydrodeoxy-compound (VI) which on dehydrogenation by palladium–charcoal gave two compounds separable by

* Part XXIX. The constitution of homolycorine and lycorenine, *J.*, 1955, 1066. Part XXX. The structure of tazettine methine, *J.*, 1955, 2962.

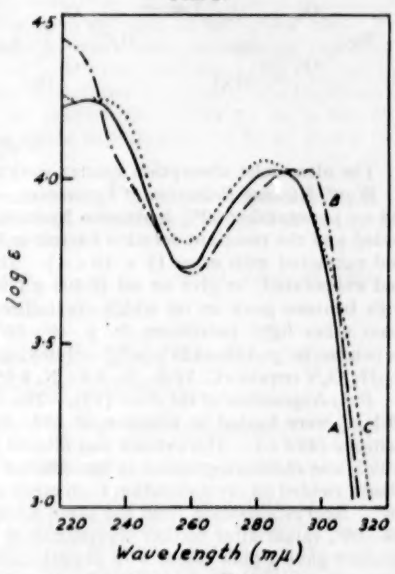
chromatography. The neutral product gave analyses correct for the expected 7-(3 : 4-dimethoxy-6-methylphenyl)-1-methylindole (VII) and exhibited the typical indole colour reactions. The second product was insoluble in acids but soluble in alkali, gave a green ferric chloride reaction, and was shown to be an indole by colour reactions: this information along with its ultimate analysis is consistent with the structure (VIII). It is interesting that it is not possible to obtain a phenol by this sequence of reactions from Wenkert's formula (II), if one excludes the unlikely possibility of a molecular rearrangement. The neutral product (VII) is closely related to the Emde base of lycorine, lycorine anhydrohydromethine (X), which we have synthesized (Humber, Kondo, Kotera, Takagi, Takeda, Taylor, Thomas, Tsuda, Tsukamoto, Uyeo, Yajima, and Yanaihara, *J.*, 1954,

FIG. 1.



Curve	Substance
A, ———	(VI)
B, – – – –	(X)
C, — — —	(XI)
D, — · — ·	(XII)

FIG. 2.

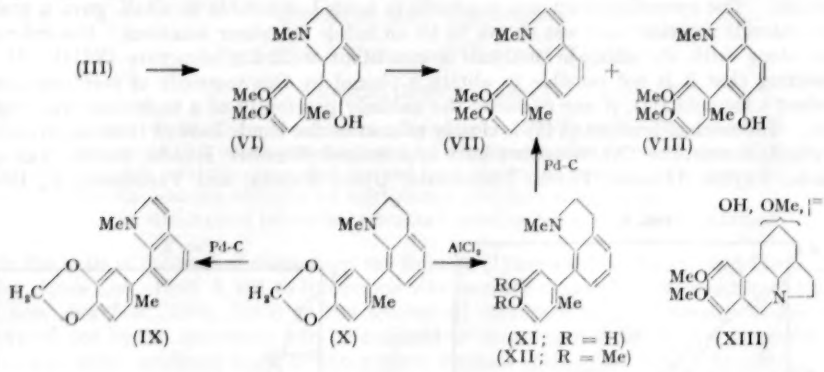


Curve	Substance
A, ———	(VII)
B, — · — ·	(IX)
C, – – – –	(VIII)

4622), and in the experiments described below this has been smoothly converted into the neutral product (VII). The base (X), when treated with aluminium chloride (Prosskurnina, *Izvest. Akad. Nauk S.S.S.R.*, 1953, **90**, 565; *Chem. Zentr.*, 1954, **125**, 1025), gave the phenolic base (XI) which ethereal diazomethane converted into the ether (XII), m. p. 69—71°. This is possibly identical with the Emde base, m. p. 69—71°, formed from galanthine (Prosskurnina, *loc. cit.*), which is closely related to lycorine and for which partial formula (XIII) has been suggested. Dehydrogenation of the ether (XII) gave the product (VII) derived from lycorenine. This synthesis also confirms the structure assigned to the phenolic product (VIII) and unequivocally establishes lycorenine as (III).

In the course of this work we have prepared the indole (IX) by catalytic dehydrogenation of the Emde base of lycorine. The ultraviolet absorption spectra of the various dihydroindoles are given in Fig. 1 and those of the indoles in Fig. 2. It is worth noting that free rotation about the bond linking the two aromatic nuclei results in spectra due to addition of the separate chromophores and different from that obtained when the rings are forced into the same plane as in 9 : 10-methylenedioxy-7*H*-dibenzo(*f*,*hi*)pyrrocoline (Cook,

Loudon, and McCloskey, *J.*, 1954, 4176), the catalytic dehydrogenation product of anhydrolycorine.



Experimental

The ultraviolet absorption spectra were measured in 95% EtOH.

Wolff–Kishner Reduction of Lycorenine.—Lycorenine (0·6 g.) was heated in diethylene glycol (14 c.c.) containing 92% hydrazine hydrate (1 c.c.) for 1·5 hr. at 130°. Sodium (0·3 g.) was added and the resultant solution heated to 190—195° for 3 hr., then diluted with water (30 c.c.) and extracted with ether (5 × 10 c.c.). The ethereal extracts were combined, dried (K_2CO_3), and evaporated, to give an oil (0·508 g.) which was chromatographed on alumina. Elution with benzene gave an oil which crystallized on trituration with ether. Two crystallizations from ether–light petroleum (b. p. 40—60°) gave the *dihydrodeoxy-compound* (VI) (0·27 g.) as prisms, m. p. 126—128°, $[\alpha]_D^{24.5}$ −146·8° (*c*, 0·374 in EtOH) (Found: C, 71·0; H, 8·2; N, 4·9. $C_{18}H_{25}O_2N$ requires C, 71·3; H, 8·3; N, 4·6%).

Dehydrogenation of the Base (VI).—The above product (0·13 g.) and 30% palladium–carbon (0·1 g.) were heated in nitrogen at 250—260° for 10 min. and the product was extracted in benzene (40 c.c.). The extract was filtered and evaporated, yielding a dark violet oil (0·118 g.) which was chromatographed in benzene on alumina. The first portion (7 c.c.) of the benzene eluate yielded on crystallization from ether–ethanol the neutral *product* (VII) (36 mg.), m. p. 94—96°. Recrystallization from the same solvent mixture gave colourless crystals (25 mg.), m. p. 98—99°, raised after further crystallization from ether to m. p. 116—118° (dimorphous). The product gave a pink colour with dimethylaminobenzaldehyde and sulphuric acid, and a positive pine splinter test (Found: C, 76·3; H, 6·7; N, 4·8. $C_{18}H_{19}O_2N$ requires C, 76·8; H, 6·8; N, 5·0%).

A phenolic *product* (VIII) was obtained by further elution with benzene, and after crystallization from ether and then methanol had m. p. 168—169°. It gave a green colour with ferric chloride and a positive Ehrlich reaction (Found: C, 72·6; H, 6·4; N, 4·8. $C_{18}H_{19}O_3N$ requires C, 72·7; H, 6·4; N, 4·7%).

Action of Aluminium Chloride on the Emde Base of Lycorine.—To a solution of this base (X) (1 g.) in chlorobenzene (16 c.c.) was added aluminium chloride (3 g.), and the mixture was heated under reflux for 3 hr. A few pieces of ice were added to the chilled mixture, the solvent was removed by steam-distillation, and the water-insoluble reddish-brown oil was extracted with ether (4 × 10 c.c.). The ether layers were concentrated to 15 c.c. and extracted with 4% aqueous sodium hydroxide (4 × 8 c.c.). The alkaline extracts were combined and saturated with ammonium chloride, and the separated phenolic material was extracted with ether (4 × 10 c.c.). The ether solutions were dried (K_2CO_3) and evaporated, to a pale yellow oil (0·526 g.) which crystallized slowly. The phenol (XI), recrystallized twice from benzene, melted at 159—161° (lit., m. p. 159—161°) and gave a green colour with ferric chloride (Found: C, 75·5; H, 6·6; N, 5·4. Calc. for $C_{16}H_{17}O_2N$: C, 75·3; H, 6·7; N, 5·5%).

Methylation of the Phenol (XI).—The phenol (0·3 g.) was set aside with ethereal diazomethane (60 c.c.) at room temperature for 4 days. After removal of the excess of diazomethane the solution was extracted with 5% hydrochloric acid (4 × 8 c.c.), the acid solutions were made alkaline with aqueous sodium hydroxide, and the non-phenolic base was taken into ether. The

ethereal solution was dried (K_2CO_3) and evaporated to dryness to an oil (0·296 g.) which solidified in ether. Recrystallization from a small amount of ether gave the *compound* (XII) (0·198 g.) as colourless cubes, m. p. 69—71° (Found: C, 76·1; H, 7·5; N, 4·9; OMe, 22·3. $C_{18}H_{21}O_2N$ requires C, 76·3; H, 7·5; N, 4·9; 2OMe, 21·9%). The *picrate* formed yellow needles, m. p. 169° (decomp.), from ethanol (Found: C, 56·5; H, 4·7; N, 11·2. $C_{18}H_{21}O_2N,C_6H_3O_7N_3$ requires C, 56·3; H, 4·7; N, 10·9%).

Dehydrogenation of the Dimethoxy-compound (XII).—This compound (0·15 g.) and 30% palladium–carbon (0·1 g.) were heated in nitrogen at 200—210° for 8 min. The product was taken up in ether (30 c.c.), and the solution filtered and washed with 5% hydrochloric acid (2 × 5 c.c.), then once with water, dried (K_2CO_3), and evaporated to a residue (0·145 g.) which crystallized slowly and melted at 102—108°. From ether, crystals (0·109 g.) were obtained having m. p. 116—118° alone or mixed with a sample of (VII) derived from lycorenine (Found: C, 77·1; H, 6·8; N, 4·8%).

Dehydrogenation of the Emde Base of Lycorine.—A mixture of the Emde base of lycorine (X) (0·2 g.) and 30% palladium–carbon (0·1 g.) was heated in nitrogen at 200° for 8 min. The product was dissolved in ether (30 c.c.), and the solution was filtered and washed twice with 5% hydrochloric acid. The ethereal layer was shaken with water, then dried (K_2CO_3), and the solvent was removed, yielding an oil (0·184 g.), which crystallized on addition of a few drops of ether. Recrystallization from ether–ethanol gave the *product* (IX) (0·139 g.), m. p. 65—67°, which gave a m. p. depression on admixture with the Emde base (Found: C, 77·0; H, 5·5; N, 5·2. $C_{17}H_{15}O_2N$ requires C, 77·0; H, 5·7; N, 5·3%).

We are indebted to Professor H. Kondo for his interest and for a gift of lycorenine and to Dr. W. I. Taylor for his advice in preparing this manuscript. We thank Mr. M. Fukuda for the microanalyses and Mr. T. Takashima for ultraviolet spectra.

School of Pharmacy, University of Osaka, Japan. [*Received, April 25th*, 1955.]

The Products from the High-temperature Reaction between Silicon Tetrachloride and Hydrogen Sulphide.

By D. J. Panckhurst, C. J. Wilkins, and P. W. Craighead.

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Silicon tetrachloride and hydrogen sulphide passed through a tube at 700—1100° yield trichlorosilanethiol, $SiCl_3{\cdot}SH$, bistrichlorosilyl sulphide, $(SiCl_3)_2S$, the compound $Si_2S_2Cl_4$, and polymeric material $(SiSCl_2)_n$. The inter-relationships of these compounds and their behaviours on thermal decomposition are reported.

When preparing trichlorosilanethiol (Wilkins and Sutton, *Trans. Faraday Soc.*, 1954, **50**, 783) it was noticed that other products besides the thiol (Pierre, *Ann. Chim. Phys.*, 1848, **24**, 286; Friedel and Ladenburg, *Annalen*, 1867, **145**, 179; *Compt. rend.*, 1867, **64**, 1295) and the crystalline dimeric "silicon sulphochloride $SiSCl_2$" (Blix and Wirbelauer, *Ber.*, 1903, **36**, 4220) arose from the high-temperature reaction between silicon tetrachloride and hydrogen sulphide. More complete examination of the crude product has led to the isolation of bistrichlorosilyl sulphide and polymeric material $(SiSCl_2)_n$. The inter-relationships of these compounds and the effect of reaction conditions upon yields have been studied. For the most part the individual chloro-sulphides constitute a series parallel to the organosilicon sulphides recently synthesised by Etienne (*Compt. rend.*, 1952, **234**, 1985; 1952, **235**, 967), who further (*Bull. Soc. chim. France*, 1953, 791) showed that the compound $Si_2S_2Cl_4$ could be obtained by condensation of silicon tetrachloride and hydrogen sulphide in the presence of an organic base. (We agree with Etienne that this compound is tetrachloro-*cyclo*disilthiane). Schumb and Bernard (*J. Amer. Chem. Soc.*, 1955, **77**, 862) recently reported a limited examination of the products of the high-temperature reaction between silicon tetrachloride and hydrogen sulphide but did not identify tetrachloro*cyclo*disilthiane.

Trichlorosilanethiol, which is obtained from the high-temperature reaction in greatest yield when the vapours are shock-cooled, is considered to be the primary product

(see Chart). Thermal decomposition of the pure thiol yields tetrachloro*cyclo*disilthiane, polymer, hydrogen sulphide, and silicon tetrachloride in proportions approximating to the scheme

$$2SiCl_3{\cdot}SH \longrightarrow H_2S + SiCl_4 + SiSCl_2 \text{ (as } Si_2S_2Cl_4 \text{ and polymer)} \quad . \quad . \quad . \quad . \quad (i)$$

A small quantity of hydrogen chloride which is also produced may arise from reaction (ii).

$$SiCl_3{\cdot}SH + SiCl_4 \longrightarrow (SiCl_3)_2S + HCl \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (ii)$$

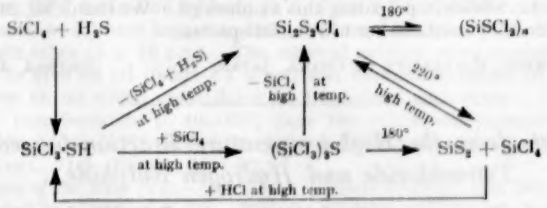
Reaction (i) may proceed by way of intermediate formation of bistrichlorosilyl sulphide, which then decomposes thermally :

$$2SiCl_3{\cdot}SH \longrightarrow (SiCl_3)_2S + H_2S \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (iii)$$

$$(SiCl_3)_2S \longrightarrow SiCl_4 + SiSCl_2 \text{ (as } Si_2S_2Cl_4 \text{ or polymer)} \quad . \quad . \quad . \quad . \quad . \quad (iv)$$

and consequently does not accumulate in the product. Evidence was obtained for the formation of bistrichlorosilyl sulphide from trichlorosilanethiol at high temperatures only when it was diluted with silicon tetrachloride. This effect may be due to repression of reaction (iv), or to facilitation of reaction (ii). Trichlorosilanethiol is catalytically decomposed with aluminium chloride at 80—100°. The reaction differs from the thermal decomposition in yielding bistrichlorosilyl sulphide but correspondingly smaller quantities of silicon tetrachloride and " $SiSCl_2$," and thus provides direct evidence for reaction (iii).

Thermal interconversion of silicon thio-chlorides.



Transformation of purified tetrachloro*cyclo*disilthiane into the liquid thio-dichloride polymer, the least volatile component of the reaction product, is rapid at 180°. At ordinary temperature the dry crystalline *cyclo*disilthiane is stable, but when moist with solvent it is very slowly transformed into the polymer. Interconversion of the constituents of the liquid polymer occurs with unusual ease even at room temperature and renders impossible isolation of successive members by fractional distillation. Polymer samples freshly obtained by heating tetrachloro*cyclo*disilthiane, or by distillation of the crude reaction product, rapidly assume a molecular weight close to that of the tetramer. During subsequent slower changes the average molecular weight passes through a maximum. Distillation of a sample whose molecular weight is close to that of, *e.g.*, the tetramer resolves the material into fractions having higher and (initially) lower molecular weights. Etienne mentions no comparable tendency of tetramethyl*cyclo*disilthiane towards polymerisation but found a small quantity of trimer $(Me_2SiS)_3$ in the product (personal communication).

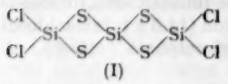
At 220° the equilibrium mixture $(SiSCl_2)_n$ undergoes disproportionation :

$$2(SiSCl_2)_n \longrightarrow nSiS_2 + nSiCl_4,$$

but some 6—7% of the chlorine is retained in the residual " silicon sulphide."

The decomposition of trichlorosilanethiol, tetrachloro*cyclo*disilthiane, and bistrichlorosilyl sulphide at relatively low temperatures suggests that, although the equilibria in the hot tube are favourable to their formation, the compounds are metastable at ordinary temperatures with respect to decomposition to silicon disulphide and silicon tetrachloride. On this view the equilibrium $Si_2S_2Cl_4 \rightleftharpoons SiS_2 + SiCl_4$, for example, should lie to the left at high temperatures, and it was in fact found that tetrachloro*cyclo*disilthiane could readily be obtained by passing silicon tetrachloride vapour over silicon sulphide at 900°. Likewise, the thiol could be obtained by passing silicon tetrachloride vapour and hydrogen chloride over silicon sulphide at 1000°.

The reaction between silicon tetrachloride and silicon sulphide also yields a secondary product $Si_3S_4Cl_4$, [probably containing some polymer $(Si_3S_4Cl_4)_n$]. This is possibly the monomer (I), the second member of the series $Si_nS_{2n-2}Cl_4$, of which tetrachloro*cyclo*disilthiane is the lowest member. It is probable that the second homologue would, like the first, polymerise through ring enlargement.



(I)

Bromination of the *cyclo*disilthiane yields dibromodichlorosilane as the only isolable silicon compound, which again accords with the symmetrical cyclic structure.

Experimental

Reaction between Silicon Tetrachloride and Hydrogen Sulphide.—Four types of run were made: (A) Silicon tetrachloride vapour and hydrogen sulphide (from ferrous sulphide; dried over $CaCl_2$), generally in the molecular ratio 12 : 1, were passed through a silica tube ($1\frac{1}{2}'' \times 36''$) heated over a 20″ length. Vapours were air-condensed and unchanged silicon tetrachloride was continuously recirculated. (B) As for (A), but the vapours were chilled by passage through an efficient water-cooled silica condenser. (C) Silicon tetrachloride vapour and hydrogen sulphide were passed in approximately equimolecular proportion through a silica tube ($1'' \times 30''$) heated over 14″, with air condensation of the vapours. The product was not recirculated. (D) As for (C), but with shock-cooling of the vapours. In all experiments silicon tetrachloride vapour was condensed from the effluent gas at −78° and returned to the system after hydrogen sulphide had been boiled off.

The products were separated by vacuum-distillation. For removal of silicon tetrachloride, trichlorosilanethiol, and bistrichlorosilyl ether the pressure was gradually reduced to about 1 mm. and the temperature increased to 50° so that the residual liquid (I, see below) boiled under reflux. The thiol (b. p. 95·5—95·6°/759 mm., m. p. −57°) was isolated by redistillation. Table 1 shows the compositions of the products from typical runs.

Table 1.

Type and no. of run	A1 [a]	A2 [b]	A3 [c]	B2 [a]	B3 [a]	B4 [a]	C	D
Temperature	950°	950°	950°	800° [d]	950°	1100°	950°	950°
H_2S flow (l./hr.)	3·5	3·5	3·5	3·5	3·5	3·5	6	6
Reaction time (hr.)	23	22	20	20	20	20	20	20
$SiCl_4$ used (g.)	750	750	750	750	750	750	750	750
$SiCl_4$ recovered (g.)	203	285	111 [e]	141 [e]	364	303	300	400
Yield of $SiCl_3{\cdot}SH$ (g.)	110	64	7	91	79	80	122	163
Higher-boiling product (total) (g.)	237	286	299	132	138	139	137	92
Yield of $(SiCl_3)_2S$ (g.)	18	18	12	15	21	34	—	—
Yield of $Si_3S_2Cl_4$ (g.)	—[g]	—[g]	173 [h]	—[g]	—[g]	—[g]	—[g]	—[g]

[a] Recirculation of trichlorosilanethiol prevented by fractionating column. [b] Unpacked column enabling recirculation of trichlorosilanethiol. [c] Unpacked column; faster recirculation from boiler, and higher (50 : 1) ratio, $SiCl_4$:H_2S. [d] The threshold temperature of the reaction is about 650°. A run at 700° gave a small yield of product of similar composition to that at 800°. [e] Considerable mechanical loss of silicon tetrachloride. [f] Not examined. [g] Low yield of tetrachloro*cyclo*disilthiane. [h] Weight of crude product before recrystallisation.

In experiments of type B yields of thiol based on the total production of silicon–sulphur compounds were almost constant over the temperature range 700—1100°. The yields of thiol from runs B and D are greater than from A and C, respectively, where shock-cooling was not used. Run D gave the highest yield of thiol, but these conditions are not necessarily maximal.

The small quantities of bistrichlorosilyl ether in the product are assumed to have arisen from attack of silicon tetrachloride on the silica tube. Packing with porcelain increased the yield of this ether but was otherwise without effect.

Bistrichlorosilyl Sulphide.—This compound can be distilled from the residue I (above), but its purification is complicated by the similar volatility of tetrachloro*cyclo*disilthiane. If present in large quantity (as in runs of type A3) much of the latter compound was removed by a preliminary crystallisation at −10°. Upon continued vacuum distillation (under about 1 mm.) bistrichlorosilyl sulphide was collected at 40—50° until the *cyclo*disilthiane began to sublime in quantity. Most of this impurity was removed by crystallisation at −50° and the remainder by discarding the residues from repeated fractional distillation. The pure compound distils at 70°/10 mm. [Found: Si, 18·7; S, 10·4; Cl, 69·8%; *M* (cryoscopic in benzene, as in all succeeding determinations), 298, 303. Calc. for Si_2SCl_4: Si, 18·65; S, 10·65; Cl, 70·7%; *M*, 301]. The compound distilled with decomposition at 187—191° at atmospheric pressure, and

when boiled under reflux for 3 hr. it decomposed almost completely into silicon sulphide and silicon tetrachloride. In an experiment to determine the course of its decomposition at higher temperatures the compound (34 g.) was passed through a clear silica tube (flushed with nitrogen) at 950° during 35 min. The products recovered were silicon tetrachloride (14·5 g.), tetrachloro-*cyclo*disilthiane (3 g.), polymer (8 g.), and unchanged bistrichlorosilyl sulphide (<5 g.). A lustrous black film formed within the heated length of the tube.

*Tetrachloro*cyclo*disilthiane and its Polymerisation.*—Distillation of bistrichlorosilyl sulphide from the crude reaction product is followed by sublimation of tetrachloro*cyclo*disilthiane (leaving residue II), but this is not readily obtained pure from preparations containing only small quantities. Larger yields were obtained from runs such as A3 in which the thiol re-circulated through the hot tube by increasing the flow of vapour from the boiler and by omitting the packing from the fractionating column. There was no significant trend in yields between 800° and 1100°. The compound was crystallised at −10° and thrice recrystallised from carbon disulphide cooled to −20° (Found: Si, 20·7; S, 24·0; Cl, 52·9%; *M*, 263, 266. Calc. for $Si_2S_2Cl_4$: Si, 21·4; S, 24·5; Cl, 54·1%; *M*, 262).

The compound melts at 80°, but after being heated for 5 hr. at 160—180° the liquid no longer crystallised on cooling. A limited quantity (7·7 g.) could, however, still be pumped from the liquid (30 g.) at or below 100° (leaving residue III). Further successive quantities of the crystalline dimer could be sublimed at 100° after re-heating to 180° at atmospheric pressure to re-establish the interconversion equilibrium. Decomposition of the liquid with formation of silicon tetrachloride commenced at 220°. In a quantitative experiment 84·9 g. of tetrachloro-*cyclo*disilthiane, heated at 220—250° for 28 hr., gave 6·2 g. unchanged or as polymer, 47 g. of silicon tetrachloride, and 30·5 g. of impure silicon sulphide (containing Cl, 7%). The decomposition is catalysed by trimethylammonium chloride.

Examination of the Least Volatile Products.—Continued distillation of residue II caused the proportion of liquid polymer passing over with the crystals to increase gradually. In the vacuum distillation of the high-boiling fraction (132 g.) from preparation B2, for example, three arbitrary fractions were taken: (1) 45—80°, chiefly crystals (7·5 g.); (2) 80—105°, crystals and liquid (60 g.); (3) 105—125°, chiefly liquid (7·5 g.). The chlorine contents of the two phases remained almost constant during the distillation, *viz.*, liquid from (2) 54·4; liquid + crystals from (2), 53·9; liquid (3), 54·3%. Towards the end of the distillation the residue rapidly thickened and solidified and some silicon tetrachloride was formed.

The Thio-dichloride Polymer.—The following molecular-weight data are typical of samples obtained by successive distillation of polymer (1) from pure tetrachloro*cyclo*disilthiane, and (2) from the crude product. (All distillations were made without causing decomposition to silicon tetrachloride or other volatile material). Unless otherwise stated, molecular-weight measurements were made immediately after isolation of the samples. (1) Residue III, obtained as above: 520, 523. (2) High-boiling distillate from runs A1 and A2 combined (Cl, 54·8%), treated as for residue III for equilibration and for removal of "dimer": 523. After distillation from a short still-head at 0·5—1 mm., measurements gave: (1) Distillate, 455 (Cl, 53·1%); residue (about one half of the distilland), 874. (2) Distillate, 468 (Cl, 55·6%). The foregoing distillates were immediately re-distilled from a steam-heated molecular still to give: (1) Distillate, 462, 537 (2 days), 632 (6 days), 563 (83 days); residue (about one third of the distilland), 748, 793 (11 days), 559 (83 days). (2) Distillate (Cl, 56·0%), 515, 589 (7 days), 466 (52 days), 393 (77 days). After 52 days 0·8 g. of 'dimer' had accumulated in 9·9 g. of this last distillate.

Material (1) distilled incompletely in the molecular still, suggesting fractionation, but material (2) distilled completely and more rapidly.

Thermal Decomposition of Trichlorosilanethiol.—Decomposition was detectable at 550° and rapid at 700°. Apart from some white solid, the products recovered after passage through a (nitrogen-flushed) silica tube are shown in Table 2. The figures for hydrogen chloride are very approximate (±25%):

TABLE 2.

$SiCl_3(SH)$ taken (mole)	Temp.	Time of passage through tube (hr.)	Products (moles)				
			$SiCl_3{\cdot}SH$	$SiCl_4$	"$SiSCl_2$" (as dimer)	H_2S	HCl
0·06	700°	1½	0·07	0·21	0·10	0·24	0·027
1·0	1100	2½	0·084	0·35	0·15	0·32	0·055
0·20 (+ 0·80 $SiCl_4$)	1100	1½	0·021	0·75	0·057	0·10	0·014

The third run differed from the first two in yielding a little liquid during the initial stages of the distillation of tetrachloro*cyclo*disilthiane. Purification of the liquid was not practicable, but analysis gave: Cl, 62·7; S, 14·7%, indicating the ratio $Si_2SCl_6 : Si_2S_2Cl_4$ within the range 1—2.

Catalytic Decomposition of Trichlorosilanethiol with Aluminium Chloride.—The thiol (0·35 mole) was heated for 4 hr. with anhydrous aluminium chloride (1·5 g.). The products were hydrogen sulphide (0·13), silicon tetrachloride (0·06), unchanged thiol (0·08), "$SiSCl_2$" (0·035, as dimer), and bistrichlorosilyl sulphide (0·06 mole) (Found: Si, 18·6; S, 10·4; Cl, 69·7%). In certain similar experiments hydrogen chloride was also evolved, the ratio $HCl : H_2S$ being 1 : 3 in one case.

Reaction between Silicon Tetrachloride and Silicon Sulphide.—Silicon tetrachloride (37·5 g.) was passed over silicon sulphide (18 g.; from thermal decomposition of the polymer) at 850—900° during 3 hr. The product was filtered and silicon tetrachloride removed. Vacuum sublimation at 70° gave tetrachloro*cyclo*disilthiane (8 g.; m. p. 78—80°) and a crystalline residue (about 3 g.) (Found: Si, 23·4; Cl, 39·5%; *M* (cryoscopic in benzene), 454. After vacuum sublimation of the product at 140° the values were: Si, 23·0; Cl, 39·9; S, 35·5%; *M*, 420. Calc. for $Si_2S_4Cl_4$: Si, 23·8; Cl, 40·0; S, 36·2%; *M*, 354).

Reaction between Silicon Tetrachloride, Silicon Sulphide, and Hydrogen Chloride.—Silicon tetrachloride (37·5 g.) and hydrogen chloride (about 5 l.) were passed over silicon sulphide (16 g.) at 1000° during 1½ hr., and the vapours shock-cooled. The condensate contained 3·5 g. of trichlorosilanethiol, b. p. 95—96°.

*Bromination of Tetrachloro*cyclo*disilthiane.*—The *cyclo*disilthiane was warmed carefully during the addition of bromine (29 g.) in small quantities. Fractionation of the product was difficult (owing probably to progressive decomposition of sulphur bromides). 23·5 g. of dibromodichlorosilane (b. p. 102—108°) were obtained, but there was no evidence of higher- or of lower-boiling silicon halides.

Analyses.—Liquid samples were weighed from a pyknometer with a ground cap, into an all-glass absorption vessel cooled in liquid air. The head of the vessel was replaced, the unit evacuated and removed from the liquid air, and the sample hydrolysed by water. Chlorine was determined by titration of strong acid (bromophenol-blue as indicator), sulphur as sulphate after hypobromite oxidation, and silicon as silica.

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The Cyclisation of 1 : 4- *and* 1 : 5-*Di*-(α-*anthraquinonylamino*)-*anthraquinones to Derivatives of Carbazole.*

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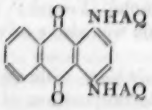
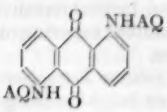
On being heated with aluminium chloride, titanium tetrachloride, or potassium hydroxide, 1 : 4-di-(α-anthraquinonylamino)anthraquinone (I) cyclises and yields the related hendecacyclic triquinone (III). The 1 : 5-isomer of (I) behaves analogously. The cyclised product (III) also results when 6-(α-anthraquinonylamino)dinaphtho(2 : 3-*a*, 2′ : 3′-*i*)carbazole-5 : 10 : 15 : 17-diquinone is heated with titanium tetrachloride. The second carbazole nucleus is formed more easily than the first. An isomeric triquinone (IV) derived from the 1 : 5-isomer is formed analogously by the action of titanium tetrachloride on the 4-(α-anthraquinonylamino)diquinone.

IN previous communications Bradley and Thitchener (*J.*, 1953, 1085) and Bradley and Butcher (*J.*, 1954, 2311) discussed the cyclisation of 1 : 1′-dianthraquinonylamine and three isomeric dibenzamido-1 : 1′-dianthraquinonylamines into 1 : 2-7 : 8-diphthaloylcarbazole and its derivatives, and the present investigation is an extension of this

work to derivatives of anthraquinone containing two α-anthraquinonylamino-substituent groups.

The formation of 1 : 4-di-(α-anthraquinonylamino)anthraquinone (I) and its conversion into a brown vat dye on being heated with potassium hydroxide, or a reddish-brown dye with aluminium chloride, were described in G.P. 208,969, 251,021, and 451,495, and the analogous conversion of 1 : 5-di-(α-anthraquinonylamino)anthraquinone (II) into brownish-

(I) 

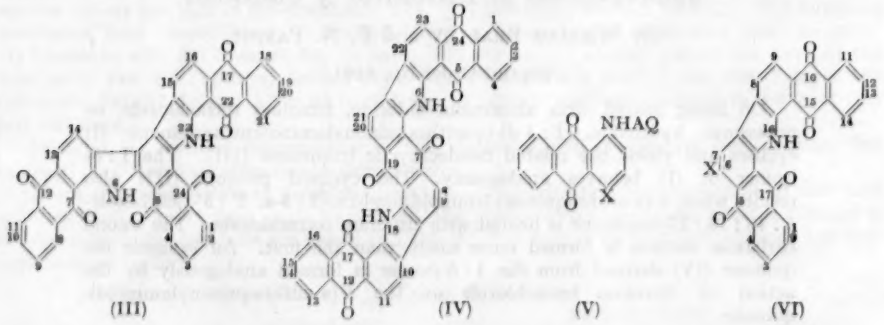
(II) 

AQ = α-anthraquinonyl.

yellow or orange dyes was described in G.P. 230,407, 240,080, 249,000, and 251,021. The structures of the products derived from (I) and (II) have not been established, but it has frequently been assumed that they are correctly represented by (III) and (IV) (see Cohn, " Die Carbazolgruppe," Georg Thieme, Verlag, Leipzig, 1919, p. 274; Thorpe's " Dictionary of Applied Chemistry," 4th edn., Vol. I, Longmans, London, p. 420; Kunz, *Melliand Textilber.*, 1952, **33**, 60), mainly because similar treatment of 1 : 1'-dianthraquinonylamine gives 1 : 2-7 : 8-diphthaloylcarbazole (literature : Bradley and Thitchener, *loc. cit.*).

The present investigation has shown that treatment of the diamine (I) with potassium hydroxide, titanium tetrachloride, or aluminium chloride under conditions described in the Experimental part gives the hendecacyclic triquinone (III), and that treatment of the isomeric diamine (II) with titanium tetrachloride as described gives the isomeric triquinone (IV). There was no evidence of nuclear hydroxylation in the action of potassium hydroxide on the 1 : 4-diamine (I), which indicates how dominant is the cyclisation process in this case (cf. Bradley and Backhouse, *J.*, 1955, 849).

In an alternative synthesis of the triquinone (III), 4-benzamido-1 : 1'-dianthraquinonylamine (V; X = NHBz) was first prepared from 1-amino-4-benzamidoanthraquinone and 1-chloroanthraquinone, and from 1-benzamido-4-chloroanthraquinone and 1-aminoanthraquinone. Hydrolysis gave 4-amino-1 : 1'-dianthraquinonylamine (V; X = NH_2), and from this was derived 4-chloro-1 : 1'-dianthraquinonylamine (V; X = Cl). Treatment with titanium tetrachloride gave 6-chlorodinaphtho(2 : 3-*a*, 2' : 3'-*i*)carbazole-5 : 10 : 15 : 17-diquinone (VI; X = Cl), and this afforded the 6-(α-anthraquinonylamino)-derivative on being heated with α-aminoanthraquinone. The end product was obtained also from 4-benzamido-1 : 1'-dianthraquinonylamine (V; X = NHBz) by cyclisation to the 6-benzamido-compound (VI; X = NHBz), hydrolysis to the 6-amino-compound (VI;



(III) (IV) (V) (VI)

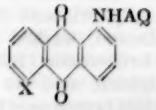
X = NH_2), and condensation of this with 1-chloroanthraquinone. The end product was identical with that prepared by the first synthesis. On being heated with titanium tetrachloride the α-anthraquinonylaminodiphthaloylcarbazole was converted into a product which had the expected properties of the triquinone (III), and was identical with

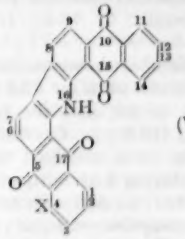
the product obtained from the diaminoanthraquinone (I) directly by treatment with aluminium chloride.

The correctness of the constitution (3-benzamido-1 : 2-7 : 8-diphthaloylcarbazole) assigned to the product from 4-benzamido-1 : 1′-di-anthraquinonylamine and aluminium chloride was established by deamination of the derived amine to 1 : 2-7 : 8-diphthaloylcarbazole, identical with the compound prepared by cyclisation of 1 : 1′-dianthraquinonylamine with aluminium chloride.

In a synthesis of the isomeric triquinone (IV), 1-benzamido-5-chloroanthraquinone and 1-aminoanthraquinone gave 5-benzamido-1 : 1′-dianthraquinonylamine (VII; X = NHBz). Treatment with aluminium chloride and pyridine gave the 4-benzamidodiquinone (VIII; X = NHBz), and thence the amino-compound (VIII; X = NH_2) by hydrolysis and the parent diphthaloylcarbazole (VIII; X = H) by subsequent deamination. The end-product was identical with 1 : 2-7 : 8-diphthaloylcarbazole prepared by the cyclisation of 1 : 1′-dianthraquinonylamine (Bradley and Thitchener, *loc. cit.*). On

(VII)





(VIII)

being heated with 1-chloroanthraquinone the amine (VIII; X = NH_2) gave the α-anthraquinonylamino-derivative (VIII; X = NHAQ), and from this was derived the triquinone (IV) by treatment with titanium tetrachloride. The end-product was identical with the product obtained directly from the diaminoanthraquinone (II) by treatment with aluminium chloride.

Experimental

Absorption spectra refer to solutions in " AnalaR " concentrated sulphuric acid.

1 : 4-*Di*-(α-*anthraquinonylamino*)*anthraquinone*.—1 : 4-Diaminoanthraquinone (15 g.), 1-chloroanthraquinone (32 g.), anhydrous potassium acetate (9 g.), and cuprous chloride (5 g.) were stirred for 20 hr. with nitrobenzene (600 c.c.) under reflux. The cooled product was washed in turn with nitrobenzene, alcohol, hydrochloric acid, and water (yield, 36·5 g.). A portion (2·5 g.) afforded on crystallisation from nitrobenzene (1·5 l.) lustrous, dark blue needles, (1·3 g.), m. p. >400° (Found: C, 77·2; H, 3·5; N, 4·3. Calc. for $C_{42}H_{22}O_6N_2$: C, 77·5; H, 3·4; N, 4·3%). Light absorption: $\lambda_{max.}$ at 265, 475, and 600 mμ. This compound appeared to be similar to that (violet needles, m. p. 410°) obtained by Ullmann and Billig (*Annalen*, 1911, **381**, 20) from 1 : 4-dichloroanthraquinone and 1-aminoanthraquinone, and that described in G.P. 208,969 according to which it was prepared from 1-bromoanthraquinone and 1 : 4-diaminoanthraquinone or the reduced form of this.

Cyclisation. Formation of the Triquinone (III).—(*a*) The above compound (3 g.) was refluxed for 3 hr. with aluminium chloride (10 g.) and pyridine (25 c.c.) in an oil-bath at 180°. Addition to water, acidification, and subsequent treatment of the solid with chromium trioxide (5 g.) and acetic acid (150 c.c.) gave a product which crystallised from quinoline in minute, brown needles (A) (Found: C, 77·6; H, 2·8; N, 4·2. Calc. for $C_{42}H_{18}O_6N_2$: C, 78·0; H, 2·8; N, 4·3%), the properties of which resembled those of the products described in G.P. 208,969 and 451,495 except that these were not obtained pure or crystalline. The product (A), 6 : 23-dihydroanthra[2′,1′,4,5]pyrrolo[1,2-*c*]dinaphtho[2,3-*a*, 2′,3′-*i*]carbazole-5 : 7 : 12 : 17 : 22 : 24-triquinone, is very sparingly soluble in organic solvents; a saturated solution in 1·5 l. of boiling nitrobenzene affords 0·1 g. of (A) on being cooled.

(*b*) 1 : 4-Di-(α-anthraquinonylamino)anthraquinone (5 g.), potassium hydroxide (50 g.), and water (5 c.c.) were heated in a nickel crucible to 260° (temperature of metal bath) during 90 min.,

care being taken to avoid frothing caused by raising the temperature too quickly. The reactants were stirred at 260° for 3 hr. and then the product was cooled and added to water (1 l.). The resulting suspension was aerated, then filtered, and the residue was washed with water and then dried (5·2 g.). It showed the same properties as the crystalline material (A) prepared as in (*a*). Oxidation with chromium trioxide in acetic acid gave an unidentified yellow product, m. p. 260°, and phthalic acid. The alkaline medium from which the cyclised product was separated was deeply coloured, but no precipitate was formed on acidification.

4-*Benzamido*-1 : 1′-*dianthraquinonylamine*.—When crystallised from nitrobenzene 1-amino-4-benzamidoanthraquinone had m. p. 287° (Battegay and Bernhardt, *Bull. Soc. chim. France*, 1923, **33**, 1510, state m. p. 278°). This derivative (34·2 g.), 1-chloroanthraquinone (24·2 g.), anhydrous sodium carbonate (6·0 g.), and copper bronze (2 g.) gave 4-*benzamido*-1 : 1′-*dianthraquinonylamine* (55 g.) after being refluxed in nitrobenzene (600 c.c.) for 24 hr. Recrystallisation from nitrobenzene gave a dark blue product (Found: C, 76·7; H, 3·6; N, 5·2. $C_{35}H_{20}O_5N_2$ requires C, 76·7; H, 3·7; N, 5·1%). Light absorption: $\lambda_{max.}$ at 257·5, 390—405, 625, 675—690 mμ. This compound was similar to that prepared from 1-benzamido-4-chloroanthraquinone and 1-aminoanthraquinone (shining dark blue needles from nitrobenzene and *o*-dichlorobenzene; Found: C, 76·5; H, 3·4; N, 5·2%) by a method similar to that of G.P. 220,581.

4-*Amino*-1 : 1′-*dianthaquinonylamine*.—The 4-benzamido-derivative (20 g.) was stirred and heated on a boiling-water bath for 4 hr. with concentrated sulphuric acid (200 c.c.). The cooled product was added to ice, and the precipitate was collected, washed with dilute aqueous ammonia, and dried (16·3 g.). Crystallisation from trichlorobenzene (1630 c.c.) gave 8·4 g. of blue needles. These were dissolved in concentrated sulphuric acid (40 c.c.), ice-cold water (15 c.c.) was added during 3 hr. with stirring, and the reddish-brown needles of the precipitated sulphate were collected, washed with 80% sulphuric acid, then hydrolysed by addition to water. 4-*Amino*-1 : 1′-*dianthraquinonylamine* crystallised from trichlorobenzene (450 c.c.) as lustrous blue needles (4·3 g.) (Found: C, 75·5; H, 3·4; N, 6·2. $C_{28}H_{16}O_4N_2$ requires C, 75·7; H, 3·6; N, 6·3%). Light absorption: $\lambda_{max.}$ at 265 and 360—365 mμ.

4-*Chloro*-1 : 1′-*dianthraquinonylamine*.—Sodium nitrite (3 g.) was added during 1 hr. to a solution of 4-amino-1 : 1′-dianthraquinonylamine (6 g.) in concentrated sulphuric acid (60 c.c.) which was stirred at 0°. After 6 hr. the resulting solution was kept 12 hr. at 0° and then added to ice. The precipitated yellow-brown diazonium compound was collected, washed with dilute hydrochloric acid at 0°, and then vigorously stirred with a solution of cuprous chloride (10 g.) in hydrochloric acid (100 c.c.). The temperature was raised to 70° during 4 hr., and then the product was collected, washed with hydrochloric acid, then with water, and finally dried (5·5 g.). Crystallisation from nitrobenzene gave lustrous, dark red needles of 4-*chloro*-1 : 1′-*dianthraquinonylamine* (Found: C, 72·5; H, 3·1; N, 2·7; Cl, 7·1. $C_{28}H_{14}O_4NCl$ requires C, 72·5; H, 3·0; N, 3·0; Cl, 7·7%). Light absorption: $\lambda_{max.}$ at 265·5 and 373·5 mμ.

4-*Nitro*-1 : 1′-*dianthraquinonylamine*.—1-Chloro-4-nitroanthraquinone (14·5 g.), 1-aminoanthraquinone (11·1 g.), anhydrous sodium carbonate (2·6 g.), and copper bronze (2·5 g.), refluxed in nitrobenzene (300 c.c.) for 24 hr., gave 4-*nitro*-1 : 1′-*dianthraquinonylamine* (21 g.) which crystallised as dark red needles (13·5 g.) from *o*-dichlorobenzene (Found: C, 71·4; H, 2·5; N, 5·4. $C_{28}H_{14}O_6N_2$ requires C, 71·9; H, 2·5; N, 5·9%). Light absorption: $\lambda_{max.}$ at 260, 430 mμ.

6-*Chlorodinaphtho*(2 : 3-a, 2′ : 3′-i)*carbazole*-5 : 10 : 15 : 17-*diquinone*.—4-Chloro-1 : 1′-dianthraquinonylamine (2 g.) was refluxed for 3 hr. with titanium tetrachloride (8 c.c.) in *o*-dichlorobenzene (40 c.c.). The cooled product was collected, washed with *o*-dichlorobenzene, then with acetone, and dried (3·2 g.). Purification from nitrobenzene (2 l.) gave a yellow solid (1·1 g.), and this was boiled for 30 min. with chromium trioxide (1·5 g.) and glacial acetic acid (100 c.c.). Crystallisation from nitrobenzene (400 c.c.) gave the 6-*chloro-compound* as lustrous yellow needles (Found: C, 72·9; H, 2·6; N, 3·2; Cl, 7·5. $C_{28}H_{12}O_4NCl$ requires C, 72·8; H, 2·6; N, 3·0; Cl, 7·7%). Light absorption: $\lambda_{max.}$ at 226, 271, and 505 mμ.

6-*Benzamidodinaphtho*(2 : 3-a, 2′ : 3′-i)*carbazole*-5 : 10 : 15 : 17-*diquinone*.—This *compound* was obtained essentially by the method of G.P. 451,495, 4-benzamido-1 : 1′-dianthraquinonylamine being cyclised by means of aluminium chloride in pyridine. The crude brown-red product was heated with alkaline sodium hypochlorite and then crystallised from nitrobenzene, giving lustrous red needles (Found: C, 76·4; H, 3·5; N, 5·6. $C_{35}H_{18}O_5N_2$ requires C, 76·9; H, 3·3; N, 5·1%). Light absorption: $\lambda_{max.}$ at 222·5—225, 264—266, 355—360, 560 mμ.

6-*Aminodinaphtho*(2 : 3-a, 2′ : 3′-i)*carbazole*-5 : 10 : 15 : 17-*diquinone*.—The above 6-benzamido-derivative (3·7 g.) was heated for 3 hr. on a boiling-water bath with concentrated sulphuric

acid (15 c.c.). The cooled product was added to ice, and the resulting precipitate was collected, washed in succession with dilute aqueous ammonia and water, and dried (2·5 g.). This material crystallised from trichlorobenzene in blue needles. Another portion (1·5 g.) was dissolved in concentrated sulphuric acid (8 c.c.). Water (2 c.c.) was added slowly and the minute yellow needles of precipitated sulphate were hydrolysed by stirring them with water. Crystallisation of the regenerated base from quinoline gave the 6-*amine* as lustrous blue needles (Found : C, 76·3; H, 3·2; N, 6·2. $C_{28}H_{14}O_4N_2$ requires C, 76·0; H, 3·2; N, 6·3%). Light absorption : $\lambda_{max.}$ at 267, 485 mμ.

Deamination to 1 : 2-7 : 8-*diphthaloylcarbazole.* Sodium nitrite (0·25 g.) was added during 30 min. to a stirred solution of the 6-amino-derivative (0·5 g.) in concentrated sulphuric acid (10 c.c.) at 0°. After 4 hr. the resulting solution was added to ice, the precipitated diazonium compound was collected, washed, and then stirred for 3 hr. with ice-cold 30% hypophosphorous acid (70 c.c.), during which frothing occurred. The suspension which remained was filtered, and the solid was washed, then dried (0·4 g.), and crystallised from nitrobenzene (350 c.c.). Yellow needles of 1 : 2-7 : 8-diphthaloylcarbazole were obtained, identical with authentic material prepared by cyclising 1 : 1′-dianthraquinonylamine with aluminium chloride (light absorption : $\lambda_{max.}$ at 226, 271, 508, and 650 mμ).

6-*Nitrodinaphtho*(2 : 3-a, 2′ : 3′-i)*carbazole*-5 : 10 : 15 : 17-*diquinone.*—A solution of the 6-amine (4 g.) in concentrated sulphuric acid (25 c.c.) was cooled to 0°. Sodium nitrite (2 g.) was added during 20 min. and stirring was continued for 4 hr. The resulting solution was added to crushed ice, the precipitated diazonium sulphate was collected, washed with ice-water, and then stirred 12 hr. with a suspension of copper sulphate in sodium nitrite [prepared by mixing aqueous solutions of sodium sulphite (10 g.) and copper sulphate (8 g.), collecting the brown precipitate, washing it free from sulphite ions, and finally suspending it in water containing sodium nitrite (20 g.)]. The suspension was heated to boiling, then filtered, and the yellow product was washed and dried (3·8 g.). After short heating with chromium trioxide in acetic acid, the product was recovered and then recrystallised several times from nitrobenzene. The 6-*nitro-compound* forms brownish-yellow needles (Found : C 71·4; H, 2·6; N, 5·8. $C_{28}H_{12}O_6N_2$ requires C, 71·2; H, 2·7; N, 5·9%).

6-(α-*Anthraquinonylamino*)*dinaphtho*(2 : 3-a, 2′ : 3′-i)*carbazole*-5 : 10 : 15 : 17-*diquinone.*—(*a*) The 6-amino-compound (1·8 g.), 1-chloroanthraquinone (0·9 g.), anhydrous sodium carbonate (0·23 g.), and copper bronze (0·2 g.) were refluxed 24 hr. with nitrobenzene (30 c.c.). The solid was collected from the cooled product and washed in turn with nitrobenzene, alcohol, hydrochloric acid, and water (yield 1·8 g.). Crystallisation from quinoline gave blue needles of the 6-α-*anthraquinonylamino-derivative* (Found : C, 77·4; H, 3·2; N, 4·6. $C_{42}H_{20}O_6N_2$ requires C, 77·8; H, 3·1; N, 4·3%). Light absorption : $\lambda_{max.}$ at 267 and 490—495 mμ. (*b*) An identical product resulted by similar condensation of the 6-chloro-compound with 1-aminoanthraquinone.

Cyclisation. The above derivative (0·5 g.) was refluxed for 3 hr. with titanium tetrachloride (1 c.c.) in *o*-dichlorobenzene (9 c.c.). The resulting solution was filtered hot, and the residue was washed in succession with *o*-dichlorobenzene and acetone, and then dried. Further treatment with alkaline sodium hypochlorite and crystallisation from quinoline gave brown needles identical in properties with compound (A).

1 : 5-*Di*-(α-*anthraquinonylamino*)*anthraquinone.*—1 : 5-Dichloroanthraquinone (27·7 g.), 1-aminoanthraquinone (45 g.), anhydrous sodium carbonate (11 g.), and copper bronze (2 g.) were heated 36 hr. under reflux in nitrobenzene (500 c.c.). The product (61 g.) was very sparingly soluble in nitrobenzene; 0·11 g. crystallised on cooling from a saturated solution in 2 l. of boiling nitrobenzene. 1 : 5-*Di*-(α-*anthraquinonylamino*)*anthraquinone* forms bright red, minute needles (Found : C, 76·4; H, 3·5; N, 4·3. $C_{42}H_{22}O_6N_2$ requires C, 77·5; H, 3·4; N, 4·3%). This description supplements the reference to the preparation of the compound which is given in G.P. 230,407.

Cyclisation. Titanium tetrachloride (40 g.) and 10 g. of the above derivative were refluxed 3 hr. in *o*-dichlorobenzene (300 c.c.). The solid (12·5 g.) was then separated, and washed with fresh solvent and finally with alcohol. It became yellow when heated at 70° with sodium hydroxide and sodium hypochlorite, and it was then similar (Found : C, 77·0; H, 2·7; N, 4·4. Calc. for $C_{42}H_{18}O_6N_2$: C, 78·0; H, 2·8; N, 4·3%) to 6 : 18-dihydrobisanthra[2′,1′,4,5]pyrrolo-[2,3-*a*, 2′,3′-*h*]anthra-5 : 7 : 12 : 17 : 19 : 24-triquinone, obtained from 1 : 5-di-(α-anthraquinonylamino)anthraquinone and potassium hydroxide (G.P. 230,407) or aluminium chloride (G.P. 240,080) after the same purification (G.P. 251,021) (substance B).

5-*Nitro*-1 : 1′-*dianthraquinonylamine.*—1-Chloro-5-nitroanthraquinone (29 g.), 1-aminoanthraquinone (23 g.), anhydrous sodium carbonate (11 g.), and copper bronze (2 g.), when refluxed

for 20 hr. in nitrobenzene (500 c.c.), gave a product (34 g.). Crystallisation from nitrobenzene (1·9 l.) gave red minute needles (22 g.) (Found : C, 71·2; H, 2·7; N, 5·2. $C_{28}H_{14}O_6N_2$ requires C, 71·9; H, 2·5; N, 5·4%) of *5-nitro*-1 : 1′-*dianthraquinonylamine*. This derivative did not yield a homogeneous product when heated with titanium tetrachloride in *o*-dichlorobenzene or with aluminium chloride in pyridine.

5-Chloro-1 : 1′-*dianthraquinonylamine*.—A solution of the 5-amino-derivative (2 g.) in concentrated sulphuric acid (10 c.c.) was diazotised at 0° by the addition of sodium nitrite (1 g.), and the resulting diazonium salt was isolated and stirred with cuprous chloride (5 g.) and hydrochloric acid (30 c.c.) for 4 hr. whilst the temperature was raised slowly from 0° to 40°. *5-Chloro*-1 : 1′-*dianthraquinonylamine* (2 g.) crystallised from *o*-dichlorobenzene in red needles, m. p. *ca.* 384° (Found : C, 72·0; H, 3·2; N, 3·3; Cl, 7·8. $C_{28}H_{14}O_4NCl$ requires C, 72·47; H, 3·0; N, 3·0; Cl, 7·7%).

Cyclisation. The chloro-compound (0·7 g.) was refluxed 2 hr. with titanium chloride (4 c.c.) in *o*-dichlorobenzene (15 c.c.). The solid was collected, washed, and boiled 1 hr. with chromium trioxide (4 g.) in acetic acid (30 c.c.) containing concentrated sulphuric acid (0·5 c.c.). The resulting *4-chlorodinaphtho*(2 : 3-a, 2′ : 3′-i)*carbazole*-5 : 10 : 15 : 17-*diquinone* (VII; X = Cl) (0·5 g.) crystallised from nitrobenzene in yellow needles (Found : C, 72·4; H, 2·8; N, 2·8; Cl, 7·4. $C_{28}H_{12}O_4NCl$ requires C, 72·8; H, 2·6; N, 3·0; Cl, 7·7%).

5-Benzamido-1 : 1′-*dianthraquinonylamine*.—1-Chloro-5-benzamidoanthraquinone (18 g.), 1-aminoanthraquinone (11·5 g.), anhydrous sodium carbonate (2·6 g.), and copper bronze (1 g.), refluxed for 24 hr. in nitrobenzene (350 c.c.), gave *5-benzamido*-1 : 1′-*dianthraquinonylamine* (27·4 g.), which formed lustrous red needles (Found : C, 76·4; H, 3·7; N, 6·0. $C_{35}H_{20}O_5N_2$ requires C, 76·7; H, 3·7; N, 5·4%).

Cyclisation. The 5-benzamido-derivative (10 g.) was vigorously stirred for 90 min. with aluminium chloride (25 g.) and pyridine (75 c.c.) in an oil-bath at 140°. The product which separated on addition to water and acidification was heated for 2 hr. at 70° with alkaline sodium–hypochlorite. The bright yellow solid was collected (9·5 g.) washed, dried, and then crystallised from nitrobenzene (6 l.). *4-Benzamidodinaphtho*(2 : 3-a, 2′ : 3′-i)*carbazole*-5 : 10 : 15 : 17-*diquinone* (VII; X = NHBz) (6 g.) formed glistening yellow needles (Found : C, 76·9; H, 3·3; N, 4·6. $C_{35}H_{18}O_5N_2$ requires C, 76·9; H, 3·3; N, 5·1%).

4-Aminodinaphtho(2 : 3-a, 2′ : 3′-i)*carbazole*-5 : 10 : 15 : 17-*diquinone*.—A solution of the 4-benzamido-derivative (1·2 g.) in concentrated sulphuric acid (10 c.c.) was heated for 4 hr. on the water-bath. The cooled solution was added to ice, and the red solid (1 g.) was crystallised from trichlorobenzene. The *amine* forms brownish-red needles (Found : C, 75·7; H, 3·4; N, 6·1. $C_{28}H_{14}O_4N_2$ requires C, 76·0; H, 3·2; N, 6·3%).

Deamination. Sodium nitrite (0·2 g.) was added during 15 min. to a solution of the 4-amine (0·35 g.) in concentrated sulphuric acid (10 c.c.) which was stirred in an ice-bath. After being stirred for 1 hr. longer the resulting solution was added to ice and kept at 0° for 2 hr., and then the precipitated diazonium salt was collected, washed (ice-water), and suspended in water (100 c.c.). Hypophosphorous acid (50 c.c. of 30%) was added; foaming occurred and a yellow precipitate was formed. The suspension was stirred overnight, the solid was collected, washed, and dried (0·32 g.), giving yellow needles of 1 : 2-7 : 8-diphthaloylcarbazole (light absorption : $\lambda_{max.}$ at 226, 271, and 508 mμ) from nitrobenzene.

4-(α-*Anthraquinonylamino*)*dinaphtho*(2 : 3-a, 2′ : 3′-i)*carbazole*-5 : 10 : 15 : 17-*diquinone*.—The above 4-amino-derivative (0·16 g.), 1-chloroanthraquinone (0·08 g.), anhydrous sodium carbonate (0·02 g.), and a small amount of copper bronze were refluxed for 24 hr. in nitrobenzene. The solid was collected from the hot suspension, and washed in turn with nitrobenzene, alcohol, hydrochloric acid, and water. The *product* crystallised from quinoline in small red needles (Found : C, 75·7; H, 3·4; N, 4·3. $C_{42}H_{20}O_6N_2$ requires C, 77·8; H, 3·1; N, 4·3%).

Cyclisation. Titanium tetrachloride (0·15 g.), and the 4-α-anthraquinonylamino-derivative (0·06 g.) were refluxed for 3 hr. in *o*-dichlorobenzene (2 c.c.). The solid was collected and then washed in turn with *o*-dichlorobenzene (2 c.c.) and alcohol. After being dried it was heated with sodium hydroxide and sodium hypochlorite; it was then identical with the product (B) prepared directly from 1 : 5-di-(α-anthraquinonylamino)anthraquinone and titanium tetrachloride.

The following Table shows colour reactions of derivatives of 1 : 1′-dianthraquinonylamine in comparison with corresponding derivatives of 1 : 2-7 : 8-diphthaloylcarbazole.

The hendecacyclic triquinone (III) derived from either 1 : 4-di-(α-anthraquinonylamino)-anthraquinone or 3-(α-anthraquinonylamino)-1 : 2-7 : 8-diphthaloylcarbazole dissolved in concentrated sulphuric acid with a dull brownish-yellow colour, unchanged on the addition of aqueous formaldehyde. The isomeric quinone (IV) gave a violet colour in concentrated

1 : 1′-Dianthraquinonylamine and its derivatives			1 : 2-7 : 8-Diphthaloylcarbazole and its derivatives		
Substituent	Colour in conc. H_2SO_4 (*a*)	Colour on addition of 40% CH_2O to (*a*)	Substituent	Colour in conc. H_2SO_4 (*b*)	Colour on addition of 40% CH_2O to (*b*)
—	Green	Dark blue	—	Red	Red
4-Chloro	Green	Royal blue	3-Chloro	Red	Red
4-Nitro	Green-yellow	Royal blue	3-Nitro	Red	Red
4-Amino	Green (red fluor.)	Deep green	3-Amino	Red	Red
4-Benzamido	Green	Green	3-Benzamido	Red	Red
4-(α-Anthraquinonylamino)	Green	Green	3-(α-Anthraquinonylamino)	Red	Red
5-Chloro	Yellow	Blue	14-Chloro	Red	Red
5-Nitro	Yellow	Blue	—	—	—
5-Amino	Yellow	Blue	14-Amino	Purple	Purple
5-Benzamido	Yellow	Blue	14-Benzamido	Blue	Blue
5-(α-Anthraquinonylamino)	Greenish-yellow	Blue	14-(α-Anthraquinonylamino)	Red-brown	Green

sulphuric acid, unchanged on the addition of aqueous formaldehyde. In 35% oleum the former product dissolved to a violet, and the latter to a deep blue solution.

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*The Synthesis of (±)-Apiose and (±)-Cordycepose.**

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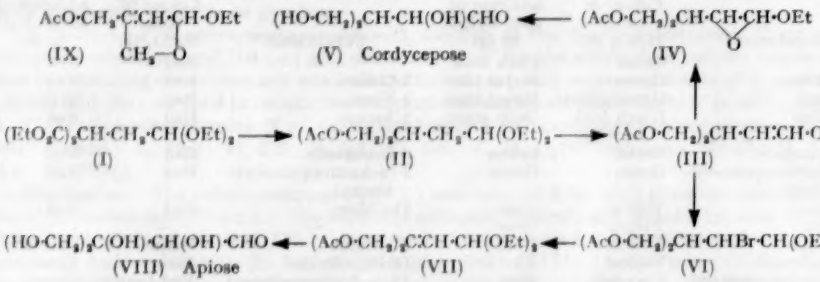
Synthetic confirmation of the structures assigned to the branched chain carbohydrates apiose (VIII) and cordycepose (V) has been obtained. The carbon skeleton is constructed by the condensation of bromoacetal with ethyl sodiomalonate to give ethyl 2 : 2-diethoxyethylmalonate (I) which, by suitable elaboration, is converted into the racemic forms of the two sugars.

FOR long the only branched-chain carbohydrate known to occur naturally was D(+)-apiose, isolated in 1900 from the glycosides of parsley (*Apium petroselinum*) (see Hudson, *Adv. Carbohydrate Chem.*, 1949, **4**, 57; Hemming and Ollis, *Chem. and Ind.*, 1953, 85) and more recently from *Posidonia australis* (Bell, Isherwood, and Hardwick, *J.*, 1954, 3702). The degradative studies of Vongerichten and Schmidt (cf. Hudson, *loc. cit.*) clearly indicated the formulation (VIII) for this sugar. Recently the closely related (−)-cordycepose was found to be the carbohydrate moiety of the glycoside cordycepin, a metabolic product of *Cordyceps militaris* (Linn.) Link (Bentley, Cunningham, and Spring, *J.*, 1951, 2301) and was shown to be 3-deoxyapiose (V) (as the stereochemistry of the cyclic structures of the two sugars is as yet incompletely elucidated, the non-committal *aldehydo*-forms of the structures are used for brevity). These structural assignments have now been confirmed by synthesis of the racemic forms of the two sugars.

Condensation of bromoacetal with ethyl sodiomalonate gave ethyl 2 : 2-diethoxyethylmalonate (I), reduced by lithium aluminium hydride to 1 : 1-diethoxy-3 : 3-di(hydroxymethyl)propane. Acetylation of this diol gave the diacetate (II). On rapid distillation of this ester from a trace of sodium hydrogen sulphate one mol. of ethyl alcohol was smoothly eliminated and 3 : 3-di(acetoxymethyl)-1-ethoxyprop-1-ene (III) was formed in high yield. This was treated with perbenzoic acid and the resulting epoxy-ether (IV) hydrolysed with aqueous-alcoholic hydrochloric acid. The (±)-cordycepose thus obtained

* A preliminary note on part of this work has already appeared (*Chem. and Ind.*, 1953, 1034).

was characterized as its *p*-nitrophenylosazone which proved to be identical with a specimen obtained from the naturally occurring sugar (we cordially thank Dr. H. R. Bentley for kindly providing a sample of cordycepin). This direct comparison of the (±)- and the



(−)-sugar is of course made possible by the elimination of the asymmetry on osazone formation.

The key compound for the synthesis of apiose was 1 : 1-di(acetoxymethyl)-2-bromo-3 : 3-diethoxypropane (VI). All attempts to prepare this by bromination of the corresponding acetal (II) were unsuccessful (cf. Simpson, *J. Amer. Chem. Soc.*, **1949**, **71**, 754; Marvel and Joncich, *ibid.*, **1951**, **73**, 973). It was obtained by addition of the elements of ethyl hypobromite (derived from a solution of *N*-bromosuccinimide in ethanol) to the enol ether (III). Dehydrobromination of the bromo-acetal (VI) with lithamide in liquid ammonia produced the corresponding unsaturated acetal (VII). This product proved to be very labile when distilled, ethyl acetate being continually evolved with the presumed production of the cyclic acetal (IX). Hydroxylation of the double bond of the acetal (VII) followed by acid hydrolysis gave crude (±)-apiose, characterised as its *p*-bromophenylosazone, identical with a sample prepared from the (+)-apiose obtained from natural sources (we are indebted to Professor Wilson Baker, F.R.S., for kindly providing this specimen).

Experimental

Ethyl 2 : 2-*Diethoxyethylmalonate* (I).—This was prepared in 64% yield as described by Perkin and Pink (*J.*, **1925**, **127**, 191). It had b. p. 108—109°/0·7 mm., n_D^{18} 1·4282.

1 : 1-*Diethoxy*-3 : 3-*di*(*hydroxymethyl*)*propane*.—To a solution of lithium aluminium hydride (9 g.) in ether (250 c.c.) was added ethyl 2 : 2-diethoxyethylmalonate (40 g.) in ether. Ice-cooling was employed to keep the mixture gently boiling. After a further 2 hours' refluxing, ethyl acetate was added, followed by water (100 c.c.). The resulting slurry was extracted with ether for 15 hr. and the extract dried (Na_2SO_4). Evaporation and distillation gave the *diol* (21·1 g., 75%), b. p. 99—103°/5 × 10^{-4} mm., 123—125°/0·05 mm., n_D^{17} 1·4511 (Found: C, 56·2; H, 10·3. $C_9H_{20}O_4$ requires C, 56·2; H, 10·5%).

3 : 3-*Di*(*acetoxymethyl*)-1 : 1-*diethoxypropane* (II).—The above diol (20 g.), acetic anhydride (33 c.c.), and pyridine (55 c.c.) were mixed and, after the initial exothermic reaction, were heated by steam for 1 hr. and set aside overnight. The mixture was poured on crushed ice (100 g.) and stirred to decompose excess of anhydride. Extraction with ether was followed by careful washing with *ice-cold* N-sulphuric acid and then sodium hydrogen carbonate solution. Drying (Na_2SO_4), evaporation, and distillation gave the *acetal* (II) (25·4 g., 88%), b. p. 122°/0·6 mm., 142°/2 mm., n_D^{15} 1·4352 (Found: C, 56·4; H, 8·8. $C_{13}H_{24}O_6$ requires C, 56·5; H, 8·75%).

A sample of the acetal was refluxed for 10 min. with a solution of 2 : 4-dinitrophenylhydrazine in aqueous acetic acid (80%). Cooling and dilution with water gave an oil that soon solidified. Crystallisation from benzene–light petroleum (b. p. 40—60°) gave 3 : 3-*di*(*acetoxymethyl*)*propanal* 2 : 4-*dinitrophenylhydrazone* as yellow plates, m. p. 56—57° (Found N, 14·7. $C_{15}H_{18}O_8N_4$ requires N, 14·65%).

In an attempt to obtain the free aldehyde, the acetal (1·75 g.) was shaken for 40 min. at 20° with tartaric acid (5 g.) in water (4 c.c.). Isolation with ether, washing with sodium hydrogen carbonate solution, drying (Na_2SO_4), evaporation, and distillation gave a product (0·55 g.), b. p. 145° (bath-temp.)/10^{-4} mm., n_D^{21} 1·4417. Analysis showed that this compound was probably 4-*acetoxymethyltetrahydro*-2-*hydroxyfuran* formed by hydrolysis of the acetal and

one acetoxy-grouping, followed by hemiacetal formation (Found : C, 52·65; H, 7·55. $C_7H_{12}O_4$ requires C, 52·5; H, 7·55%).

3 : 3-*Di*(*acetoxymethyl*)-1-*ethoxyprop*-1-*ene* (III).—In a 100-c.c. flask fitted with a wide-bore, short stillhead without fractionating column was placed 3 : 3-diacetoxymethyl-1 : 1-diethoxypropane (15·4 g.), sodium hydrogen sulphate (0·05 g.; freshly fused and powdered), and a few porous chips. With the apparatus evacuated to 0·5 mm. the flask and contents were immersed in an oil-bath preheated to 110° and the temperature of the bath then increased to 140° as rapidly as the copious frothing allowed. After 4 minutes' heating distillation began and, carried out as quickly as possible (bath-temp. 140—160°), was substantially complete in 5 min. Fractionation of the distillate (12·2 g.) gave 3 : 3-*di*(*acetoxymethyl*)-1-*ethoxyprop*-1-*ene* (10·6 g., 83%), b. p. 95—97°/0·4 mm., n_D^{20} 1·4446 (Found : C, 57·0; H, 7·3. $C_{11}H_{18}O_5$ requires C, 57·4; H, 7·9%). Treatment with an aqueous-acetic acid solution of 2 : 4-dinitrophenylhydrazine gave the 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 56—57°, described above. This demonstrated that no skeletal rearrangement had occurred during pyrolysis.

(±)-*Cordycepose* (V).—The above enol ether (III) (1 g.) was treated with a solution of perbenzoic acid (0·6 g., 1 mol.) in chloroform (34 c.c.) and set aside at 0° for 24 hr. The solvent was removed under reduced pressure and the residue heated by steam for 1 hr. with ethanol (10 c.c.) and hydrochloric acid (2N; 25 c.c.). The cooled mixture was shaken with benzene (3 × 20 c.c.), and the aqueous layer diluted to 70 c.c. with water. Passage through a column of anion-exchange resin (Amberlite IR-4B pre-saturated with carbon dioxide), followed by evaporation to dryness under reduced pressure, gave a brown syrup (0·46 g.) which was dissolved in a little methanol and filtered twice through a charcoal pad. The filtrate was evaporated to dryness and the residue dissolved in water (1 c.c.), washed with ether, evaporated to dryness under reduced pressure, and dried (P_2O_5) for 18 hr. at 0·5 mm. The product, (±)-cordycepose, was a colourless syrup (Found : C, 45·6; H, 8·1. $C_5H_{10}O_4$ requires C, 44·8; H, 7·5%).

A sample of the sugar (42 mg.) in hydrochloric acid (2N; 2 c.c.) was treated with *p*-nitrophenylhydrazine (0·3 g.) in hydrochloric acid (2N; 5 c.c.). After 4 hr. at room temperature a little sticky solid was filtered off and discarded. Thereafter the solid slowly precipitated and was collected daily for 10 days, washed with water, and dried. Crystallisation of this product (55 mg.) from nitromethane gave cordycepose *p*-nitrophenylosazone as a dark-red microcrystalline powder, m. p. 259—260° (Kofler block) undepressed on admixture with a specimen derived from acid-hydrolysed cordycepin. A mixture of the synthetic and the naturally derived osazone gave a single sharp band when developed in ethyl acetate on alumina.

Attempted preparation of the *p*-bromophenylosazone following Bentley, Cunningham, and Spring's directions (*loc. cit.*) gave cream-coloured clustered blades, m. p. 162—163° (from water), as recorded by them. This compound, however, proved to be, not the expected osazone, but *N*-acetyl-*p*-bromophenylhydrazine, undepressed on admixture with a sample prepared by heating the hydrazine with dilute acetic acid (Found : C, 41·8; H, 4·1; N, 12·3. Calc. for $C_8H_9ON_2Br$: C, 41·95; N, 4·0; N, 12·2%). The calculated analytical figures for the osazone and the *N*-acetyl derivative are very close and thus conducive to misconception.

1 : 1-*Di*(*acetoxymethyl*)-2-*bromo*-3 : 3-*diethoxypropane* (VI).—Finely powdered *N*-bromosuccinimide (4·3 g.; dried over P_2O_5 for 1 hr. at 50°/10^{-4} mm.) was added gradually during 20 min. to a vigorously stirred, cooled (−3°) solution of 3 : 3-di(acetoxymethyl)-1-ethoxyprop-1-ene (III) (5·3 g.) in dry ethanol. Stirring was continued for 45 min. at −3° and then for 2 hr. at room temperature. The succinimide formed was filtered off, ether (150 c.c.) added, and the solution well shaken with sodium hydrogen carbonate solution (5 × 60 c.c.) and water until the washings were neutral. Drying ($MgSO_4$), evaporation, and fractionation gave 1 : 1-*di*(*acetoxymethyl*)-2-*bromo*-3 : 3-*diethoxypropane* (3·9 g., 48%), b. p. 119—122°/0·35 mm., n_D^{18} 1·4630 (Found : C, 43·7, 43·4; H, 6·0, 6·3. $C_{13}H_{23}O_6Br$ requires C, 43·95; H, 6·5%).

1 : 1-*Di*(*acetoxymethyl*)-3 : 3-*diethoxyprop*-1-*ene* (VII).—A solution of the bromo-acetal (VI) (5·3 g.) in dry ether (20 c.c.) was added rapidly to a well-stirred suspension of lithamide (from lithium, 0·5 g.; formation catalysed by ferric nitrate) in liquid ammonia (250 c.c.) contained in a well-lagged flask. After 30 min. ammonium nitrate (7 g.) was added and the ammonia allowed to evaporate overnight; remaining traces of ammonia were removed under reduced pressure at 30°. The residue was extracted with ether (4 × 40 c.c.); drying, evaporation, and distillation gave a main fraction of ethylenic material (2·4 g.), b. p. 88—100°/0·4 mm., n_D^{18} 1·4544—1·4595. Rapid fractionation gave the substantially pure unsaturated *acetal* (VII) (1·5 g., 37%), b. p. 90—93°/0·5 mm., n_D^{18} 1·4540 (Found : C, 55·3; H, 8·15. $C_{13}H_{22}O_6$ requires C, 56·9; H, 8·1%). If distillation was prolonged, ethyl acetate was evolved with the production of the cyclic acetal (IX); this transformation accounts for the unsatisfactory analytical figures.

(±)-*Apiose* (VIII).—The unsaturated acetal (VII) (1·35 g.) was dispersed by vigorous stirring in ice-water (30 c.c.) through which carbon dioxide was rapidly bubbled. Aqueous potassium permanganate (2%; 30 c.c.) was then added dropwise during 50 min. at 0—3° (cooling). The mixture was then allowed to rise to 7° and a few drops of ethanol added to destroy excess of permanganate. After the precipitate had coagulated, it was filtered off and the filtrate passed through a cation-exchange resin (Amberlite IRC-50) to remove potassium. After ether-extraction the effluent and washings (200 c.c.) were treated with concentrated hydrochloric acid (2 c.c.) and hydrolysis allowed to proceed at room temperature for 24 hr. Passage through an anion-exchange resin (Amberlite IR-4B pre-saturated with carbon dioxide), followed by evaporation to dryness under reduced pressure at room temperature, gave crude (±)-apiose (0·53 g., 78%).

A mixture of this product (90 mg.), *p*-bromophenylhydrazine (180 mg.), water (2 c.c.), and 50% acetic acid (0·6 c.c.) was heated by steam. A brown oil began to separate almost immediately. After 90 minutes' heating the pale yellow supernatant liquor was decanted while still hot; on being cooled it deposited crystals of *N*-acetyl-*p*-bromophenylhydrazine. The remaining brown product was washed with water and dissolved in ethyl acetate to remove tar. This solution was washed with water, then evaporated to dryness, and the residue azeotropically dried by adding benzene and distilling off some of the solvent. The benzene-insoluble residue (*N*-acetyl-*p*-bromohydrazine) was filtered off and the reddish-brown benzene solution reduced in volume to 0·5 c.c. After 24 hr. at room temperature this solution deposited yellowish-brown granules (41 mg.), m. p. 188—196°. Recrystallisation from ethanol gave apiose *p*-bromophenylosazone as tiny bright yellow needles, m. p. 206—208° (Kofler block) undepressed on admixture with a sample of the same m. p. derived from natural sources. The *X*-ray powder photographs of the synthetic and the naturally derived osazones were identical (we cordially thank Professor J. M. Robertson, F.R.S., for arranging these determinations).

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Mass-law and Ionic-strength Effects in the Hydrolysis of Dichlorodiphenylmethane.

By B. Bensley and G. Kohnstam.

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The rate of hydrolysis of dichlorodiphenylmethane is controlled by the rate of heterolysis of one of the C–Cl linkages. This process involves the unimolecular mechanism, S_N1, and is subject to the operation of significant mass-law and ionic-strength effects (cf. Hughes, Ingold, *et al.*, *J.*, 1940, 979). The rate of ionisation and the mass-law constant are larger than for chlorodiphenylmethane under similar conditions, and the ionic-strength constant is less. These observations are consistent with electron-donation by the α-chloro-substituent towards the reaction centre.

The energy of activation for the reaction of the carbonium ion, Ph_2ClC^+, with chloride ions is about 1 kcal. less than for its hydrolysis. The ionic recombination can also be expected to be the more sensitive to changes in the solvent composition and this is considered to account for the observed increase of the mass-law constant as the ionising power of the solvent is reduced.

In aqueous acetone, any contribution to the overall reaction due to the direct solvolysis of ion-pairs (Winstein *et al.*, *Chem. and Ind.*, 1954, 664) is negligibly small.

This paper reports a kinetic investigation of the hydrolysis of dichlorodiphenylmethane and the effect of salt additions on the rate. It has long been known that this reaction occurs fairly readily with the formation or benzophenone (Kekulé and Franchimont,

Ber., 1872, **5**, 908). More recently, the solvolysis in ethanol has been investigated by Andrews and Kaeding (*J. Amer. Chem. Soc.*, 1951, **73**, 1007) who found that the reaction followed first-order kinetics, the rate being greater than for monochlorodiphenylmethane by a factor of about 15, and unaltered by the addition of ethoxide ions. The rate-determining stage, the heterolysis of one of the C–Cl linkages, must therefore involve the unimolecular mechanism, S_N1, (cf. Hughes, *Trans. Faraday Soc.*, 1941, **37**, 603) and there is no reason to assume a different mechanism in the reaction with water.

Hughes, Ingold, and their co-workers (*J.*, 1940, 960 *et seq.*; 1952, 2488 *et seq.*) have shown that S_N1 solvolysis of the C–Cl bond is associated with the operation of mass-law and ionic-strength effects which are characteristic of this mechanism and may lead to appreciable deviations from the first-order rate law. In the absence of added salts these effects are more apparent in hydrolysis than in ethanolysis (cf. Hughes, Ingold, and Taher, *J.*, 1940, 949) and the present investigation aimed at establishing the influence of an α-chloro-group on their magnitude.

Experimental

Preparation of Materials.—Dichlorodiphenylmethane was prepared by the conventional method from phosphorus pentachloride and benzophenone (Gattermann and Schultz, *Ber.*, 1896, **29**, 2944; Andrews and Kaeding, *loc. cit.*). The hydrolysable chloride of two different samples was 99·6% and 99·8% of the theoretical amount.

Chlorodiphenylmethane was prepared by the method of Hughes, Ingold, and Taher (*loc. cit.*). The hydrolysable chloride was 99·8% of the theoretical amount.

Acetone was obtained from the commercial product by Conant and Kirner's method (*J. Amer. Chem. Soc.*, 1924, **46**, 245) and fractionated through a 20-plate column. The addition of 250 ml. of water to 750 ml. of this acetone gave " 75% " aqueous acetone, and the other solvent, " 85% " aqueous acetone, was prepared in an analogous manner.

Inorganic chlorides and bromides, which were added to some of the reaction mixtures, were dried *in vacuo* over phosphoric oxide at elevated temperatures, " AnalaR " products being used when possible.

Products of Hydrolysis.—Dichlorodiphenylmethane (0·2214 g.) was allowed to react in the " 85% " solvent. After completion of the reaction, the solution was made alkaline with ammonia and most of the acetone pumped off. The remaining mixture was poured into an excess of ice-water, and the precipitated product filtered off, washed, dried over phosphoric oxide, and weighed. 0·1624 g. of product was obtained (calc. for benzophenone 0·1701 g.), having m. p. and mixed m. p. 47·5°. Extraction of the residues with ether failed to yield any further product.

There was no evidence for any reversibility of the hydrolysis. The acidity of a mixture of hydrochloric acid and benzophenone in the " 85% " solvent did not change for 24 hr. at 25°.

Rate Measurements.—The hydrolysis of dichlorodiphenylmethane was examined at 0° and 24·76°, the thermostats being of conventional design. The inital concentrations varied from 0·0025 to 0·02M. When inorganic halides were added the ionic strength at complete reaction was never greater than 0·06; usually it was much less. In a kinetic run the appropriate amount of the organic chloride was added to the solvent after this had attained the thermostat temperature, and samples (5 ml.) were withdrawn from time to time, run into cold, neutral acetone (200 ml.) to stop the reaction, and titrated with standard sodium hydroxide (lacmoid as indicator). The first reading was taken as " zero time " and the initial concentration of dichlorodiphenylmethane obtained from the " infinity " reading, *i.e.*, after more than 10 half-lives had elapsed. The concentration of any salt added to the reaction mixture was determined argentometrically, except when chlorides and bromides were added together. Such solutions were made up by weight. Several batches of the two solvents were employed and each batch was monitored by examining the rate of hydrolysis of chlorodiphenylmethane (good first-order kinetics were observed for initial concentrations of 0·02M), the necessary correction being applied to the runs with the dichloride.

Integrated first-order rate coefficients (integrated rates, $\bar{k}_1$) were calculated from the experimental results by means of the equation $\bar{k}_1 t = \ln (a/a - x)$, where the symbols have their usual meaning. Initial rates, $(k_1)_0$, were obtained from these quantities by extrapolation to " zero time." The subscript 0 will be used throughout this paper to refer to values at " zero time."

Results.—The kinetic form of the hydrolysis of dichlorodiphenylmethane is illustrated below

for reaction in the " 75% " solvent at 0° with $[Ph_2CCl_2]_0 = 0.0164$ (Run 3). 5 ml. of the reaction mixture were titrated with 0·01109N-sodium hydroxide; t is in sec., $\bar{k}_1$ in sec.$^{-1}$.

$10^{-3}t$ ...	0·000	0·240	0·540	0·840	1·1145	1·460	1·750	2·040	2·355	2·680	3·100	3·515	∞
Titre...	0·84	2·02	3·30	4·30	5·23	6·03	6·71	7·31	7·90	8·40	9·10	9·70	15·39
$10^4\bar{k}_1$...	—	3·512	3·430	3·232	3·135	3·020	2·952	2·883	2·820	2·735	2·705	2·672	—

It is seen that $\bar{k}_1$ decreases as the reaction proceeds. Similar results were observed even when the initial concentration was as low as 0·0024M (cf. Table 3), in the presence of inorganic bromides, and also in the " 85% " solvent. When ionised chlorides were added to the reaction mixture this decrease became progressively less as the salt concentration increased (cf. Table 4).

The initial rate was not independent of the initial concentration of the organic chloride. This is illustrated in Table 1 where it is shown that this is entirely due to the retarding effect of the chloride ions which are inevitably formed in the time interval between the mixing of the reactants and the first reading at " zero time." The initial rate depends only on $[Cl^-]_0$ and is independent of $[Ph_2CCl_2]_0$.

TABLE 1. *The effect of initial concentration on the initial rate* $[(k_1)_0$ *in sec.*$^{-1}]$.

Runs F, 4, and G were carried out in the " 75% " solvent at 0°; 25, 23, and V in the " 85% " acetone at 24·76°.

Run	Addition	$[Ph_2CCl_2]_0$	$[Cl^-]_0$	$10_4(k_1)_0$	Change (%)
F	—	0·00237	0·00026	4·35	—
4	—	0·01600	0·00250	3·75	−16
G	LiCl, 0·00228M	0·00241	0·00249	3·70	−17
25	—	0·00260	0·00045	7·55	—
23	—	0·01540	0·00280	5·80	−23
V	LiCl, 0·00226M	0·00242	0·00252	5·90	−21

It is of interest that the retardation of the reaction by chloride ions is more marked in the less aqueous solvent.

The effect of added salts, at 0·0165M, on the initial rate $[(k_1)_0$ in sec.$^{-1}]$ is illustrated below for reaction in the " 75% " solvent at 0° with $[Ph_2CCl_2]_0 = 0.016$M:

Added salt	—	NaBr	NaCl
$10^4(k_1)_0$	3·75	4·15	2·40

These results are quite general; ionised bromides accelerate the reaction, chlorides retard it.

When chloride and bromide ions were present in the same reaction mixture at ionic strength 0·0515, the initial rate in the " 75% " solvent at 0° followed the relation

$$10^4(k_1)_0 = 4{\cdot}820/(1 + 36{\cdot}9[Cl^-])$$

This is demonstrated in Table 2 where the values thus calculated are compared with those observed.

TABLE 2. *Initial rates at constant ionic strength in* " 75% " *aqueous acetone at* 0°.

$[Ph_2CCl_2]_0 \sim 0.005$, $[KCl] + [KBr] = 0.0507$, $[Cl^-]_0 = [KCl] + 0.0008$,* $0{\cdot}80 \leqslant 10^3\,[Cl^-]_0 \leqslant 26{\cdot}2$.

$10^3[Cl^-]_0$	0·80	5·88	10·95	16·02	21·10	26·20
$10^4(k_1)_0$, obs.	4·71	3·91	3·44	3·04	2·71	2·45
$10^4(\bar{k}_1)_0$, calc.	4·68	3·96	3·43	3·03	2·71	2·45

* Due to hydrolysis before the first reading. This quantity was constant within ± 0·0001.

All these results are fully consistent with an S_N1 reaction subject to the operation of a powerful mass-law effect.

Mass-law and Ionic-strength Constants.—(a) *Calculations.* α°, the mass-law constant, and σ, the ionic-strength constant, were calculated by means of the equation of Bateman, Church, Hughes, Ingold, and Taher (*J.*, 1940, 979, eqn. 14). For the hydrolysis of dichlorodiphenylmethane this equation can be written in the form

$$\frac{d[Ph_2CO]}{dt} = \frac{k_1^\circ[Ph_2CCl_2]}{\alpha^\circ[Cl^-]\ \text{antilog}_{10}(A\mu^{\frac{1}{2}}) + \text{antilog}_{10}(B\sigma\mu)} \quad . \quad . \quad . \quad \text{(i)}\ *$$

* This equation was employed in all calculations though, strictly, it is not applicable in the presence of bromide ions where the processes $R^+ + Br^- \rightleftharpoons RBr$ should be taken into account. Alkyl bromides, however, are known to undergo ionisation much more rapidly than the corresponding chlorides and it therefore appeared reasonable to apply the stationary-state principle to RBr. Under these conditions the resulting rate equation is easily shown to be identical with equation (i).

where k_1° is the rate constant, at zero ionic strength, of the rate-determining ionisation $Ph_2CCl_2 \longrightarrow Ph_2ClC^+ + Cl^-$, $A = -1{\cdot}815 \times 10^6(DT)^{-3/2}$, $B = -0{\cdot}912 \times 10^8(DT)^{-\frac{1}{2}}$ and μ, D, and T are the ionic strength, dielectric constant, and absolute temperature, respectively.

Writing $[Ph_2CO] = x$, $[Ph_2CCl_2]_0 = a$, $[Cl^-]_0 = c$, and $[Br^-]_0 = b$, we have $[Ph_2CCl_2] = a - x$, $[Cl^-] = c + 2x$, and $\mu = b + c + 2x$.

The integrated form of equation (i) can then be written in the form

$$I/t = k_1^\circ + \alpha^\circ (J/t) \quad \text{. . . . . (ii)}$$

where $$I = \int_0^x \frac{\text{antilog}_{10}\, B\sigma(b + c + 2x)}{a - x} \cdot dx$$

and $$J = \int_0^x \frac{(c + 2x)\ \text{antilog}_{10}\, A(c + b + 2x)^{\frac{1}{2}}}{a - x} \cdot dx$$

Equation (ii) contains three unknown parameters: σ (in the integral I), k_1°, and α°. If σ is known the other two may be obtained from the results of any one run as the slope and intercept of the straight line I/t as a function of J/t. Now, σ can be expected to be of the order of 10^{-8} (*idem, loc. cit.*) and B is 1—2×10^8 under our experimental conditions. The error in the integral I caused by taking σ as zero will therefore be very small in the most dilute solutions employed where $b = c \simeq 0$, $2x \leqslant 0{\cdot}005$. In the first place, k_1° and α° were therefore determined from the results observed in such reaction mixtures on the assumption that σ was zero. That value of σ which led to the same values for these parameters at the highest ionic strength employed, ($b + c = 0{\cdot}05$, $2x \leqslant 0{\cdot}01$), was then used for their recalculation from the results in the dilute solutions. This procedure did not significantly change their value. The σ thus obtained was therefore accepted and utilised in their calculation from the results observed in other reaction mixtures. The method of least squares was employed in each case to give the "best" straight line, A and B being evaluated from Akerlof's data for the dielectric constants of acetone–water mixtures (*J. Amer. Chem. Soc.*, 1932, **54**, 4125). The integral I was obtained from the expression

$$I = (\bar{k}_1 t - 4{\cdot}606\, B\sigma x)\,\text{antilog}_{10}\, B\sigma(b + c + 2a)$$

which represents the first two terms of the series for that integral, the contribution of all other terms being negligibly small; $\bar{k}_1$ is the integrated first-order rate coefficient. J was obtained by graphical integration.

The values of these integrals in a typical run are given in Table 3.

TABLE 3. *Reaction of dichlorodiphenylmethane in "75%" aqueous acetone at 0° (Run F).*

$a = 0{\cdot}002365$, $b = 0$, $c = 0{\cdot}000263$; $A = 1{\cdot}588$, $B\sigma = -0{\cdot}8402$.

t *	10^4x †	$10^4\bar{k}_1$ ‡	$10^7J/t$ §	$10^4I/t$ ‡	t *	10^4x †	$10^4\bar{k}_1$ ‡	$10^7J/t$ §	$10^4I/t$ ‡
230	2·19	4·226	1·810	4·220	2040	12·94	3·885	5·638	3·869
540	4·82	4·218	2·703	4·210	2405	14·39	3·899	6·050	3·882
835	6·98	4·116	3·406	4·107	2760	15·48	3·853	6·720	3·834
1125	8·65	4·046	4·100	4·036	3180	16·64	3·825	7·200	3·807
1440	10·34	3·990	4·708	3·978	3610	17·61	3·780	7·560	3·761
1745	11·83	3·973	5·280	3·959					

$k_1^0 = 4{\cdot}376 \times 10^{-4}$ sec.$^{-1}$, $\alpha^\circ = 81$ mole^{-1} l.

* Sec. † Mole l.$^{-1}$. ‡ Sec.$^{-1}$. § Mole l.$^{-1}$ sec.$^{-1}$.

When ionised chlorides had been added to reaction mixtures, the variation of J/t was small over the course of the run. Under these conditions, the value obtained for k_1° was liable to considerable inaccuracy as its determination now involved extrapolation over a much greater range than that covered by the experimental points. For such systems the value of k_1° from other experiments was accepted, and only α° was calculated by means of equation (ii). This is illustrated in Table 4.

Our method for the calculation of α° and k_1° differs from that previously employed (Bateman *et al.*, *loc. cit.*) where k_1° was obtained from the initial rates in the absence of added salts. In view of the marked effect of even small quantities of chloride ions on the rate (cf. Table 1), this procedure would only have been valid for the most dilute solutions where the accuracy was not of the highest order. The relatively small effect of changes in σ on the results of this investigation also led us to prefer the present method which, here, gives more accurate values of α°.

TABLE 4. *Reaction of dichlorodiphenylmethane in "* 85% *" aqueous acetone at* 24·76° *in the presence of* LiCl (*Run U*).

$a = 0{\cdot}002712$, $b = 0$, $c = 0{\cdot}005144$; $A = 2{\cdot}307$, $B\sigma = -1{\cdot}382$, $10^4k_1^\circ = 8{\cdot}08$ * sec.$^{-1}$. Units as in Table 3.

t	10^4x	$10^4\bar{k}_1$	$10^6J/t$	$10^4I/t$	α°	t	10^4x	$10^4\bar{k}_1$	$10^6J/t$	$10^4I/t$	α°
175	2·35	5·160	1·894	5·090	(158)	1920	16·71	4·997	2·249	4·900	142
415	5·30	5·245	2·005	5·172	146	2240	18·22	4·981	2·295	4·888	139
675	8·03	5·204	2·074	5·125	143	2520	19·24	4·916	2·302	4·825	142
895	9·96	5·118	2·096	5·035	146	2825	20·27	4·872	2·325	4·770	143
1330	13·33	5·088	2·172	5·002	142	3170	21·34	4·844	2·355	4·740	142
1600	15·07	5·072	2·225	3·991	139						

α° (mean) = 142·5.

* This refers to the solvent employed in the present experiment. The value quoted later in this paper, 7·780, applies to a different batch of solvent.

(b) *Results.* In "75%" aqueous acetone at 0°, $\sigma = 1{\cdot}1 \times 10^{-8}$, and it was assumed that the same value applied in the "85%" solvent. This figure is subject to an error of 5—10% as changes in the magnitude of σ had only a relatively small effect on k_1° and α° under the existing experimental conditions. For example, in the "75%" solvent at 0°, with the ionic strength at 0·05, the term involving this parameter (the integral I) is only altered by 25% when its value is reduced to zero.

The mean values of k_1° (in sec.$^{-1}$) and α° (in mole^{-1} l.), together with their standard deviations, are given below for the experiments carried out in the "75%" solvent at 0°. The initial concentration of the organic chloride varied in the range 0·0025—0·02, any salts added were at 0·002—0·05M, and the ionic strength was never greater than 0·06:

(i) No addition, or + LiBr, NaBr, KBr; 12 experiments:

$$10^4k_1^\circ = 4{\cdot}386 \pm 0{\cdot}053,\ \alpha^\circ = 80{\cdot}3 \pm 3$$

(ii) + LiCl, HCl, NaCl, KCl + KBr; 16 experiments:

$$\alpha^\circ = 78{\cdot}7 \pm 2$$

The consistent results obtained in this solvent confirm the value of σ which was calculated from a smaller number of experiments and also show that equation (i) is applicable under these conditions.

The investigation of the reaction in the "85%" aqueous acetone was not as extensive as in the more aqueous solvent. In the absence of added salts the following results were obtained:

(iii) At 24·76°, $[Ph_2CCl_2]_0 = 0{\cdot}0025$ or 0·016, 8 experiments:

$$10^4k_1^\circ = 7{\cdot}780 \pm 0{\cdot}276,\ \alpha^\circ = 140{\cdot}3 \pm 5{\cdot}5$$

(iv) At 0°, $[Ph_2CCl_2]_0 = 0{\cdot}005$, 2 experiments:

$$10^4k_1^\circ = 0{\cdot}530\ (\pm 0{\cdot}001),\ \alpha^\circ = 126\ (\pm 6).$$

The probable error in k_1° is greater than before but it can be reduced a little by the choice of a slightly lower value for σ than in the "75%" solvent. In view of the lack of sufficient experimental results it is difficult to justify such a procedure which, in any case, does not appreciably alter α°. In the presence of small quantities of lithium chloride ($\leqslant$0·005M) α° is the same as in the absence of added electrolytes, but its value increases with increasing salt concentration. Thus for [LiCl] = 0·0040, $\alpha^\circ = 142$, and for [LiCl] = 0·0215, $\alpha^\circ = 155$; and a reasonable reduction of σ does not reduce this increase to any significant extent. Hughes, Ingold, and their co-workers (*locc. cit.*) have pointed out that equation (i) is, strictly, applicable only to very dilute solutions as it involves assumptions similar to those of Debye's limiting theory of the activity coefficients of electrolytes. These assumptions become increasingly less justified as the ionic strength is increased or the dielectric constant of the solvent reduced. Under these conditions the ionic activity coefficients are too low and hence the integrals I and J, which contain these quantities, also have too small a value. In these experiments α° was evaluated from the expression $\alpha^\circ = (k_1^\circ t - I)/J$; any factor which tends to make I and J too small will therefore tend to increase α°, and our observations in the presence of the larger quantity of lithium chloride are consistent with this prediction. Similar deviations from equation (i), arising from an underestimate of the ionic activity coefficients, have already been reported in this solvent (*idem, locc. cit.*) though they became apparent at rather higher values of the ionic

strength than here. This is probably because the present method allows a more sensitive check of the applicability of this equation. The absence of such deviations in the more aqueous solvent is considered to result from its greater ionising power.

The conductance of lithium bromide solutions (Olson and Konecny, *J. Amer. Chem. Soc.*, 1953, **75**, 5801) leads to the conclusion that this salt is almost completely dissociated in "75%" aqueous acetone, but not in the "85%" solvent. If lithium chloride can be expected to be a weaker electrolyte than the bromide (Spieth and Olson, *ibid.*, 1955, **77**, 1412), the value of J (calculated on the assumption of complete ionisation) is subject to two errors: incomplete ionisation implies an overestimate of the ionic strength and thus tends to reduce J below its real value, but the concomitant overestimate of the chloride-ion concentration tends to make J too large. It can easily be shown that the second factor has the greater effect on J, which should therefore be too large. As a first approximation the error in I can be neglected,* and incomplete dissociation of lithium chloride should therefore lead to a reduction of α°. This is not consistent with the observed increase in this parameter on the addition of this salt.

Two experiments in the presence of lithium bromide, however, showed a decrease in α°, and an increase in k_1°, with increasing salt concentration. The same arguments can be employed to show that this cannot be due to an underestimate of the ionic activity coefficients, and that this result is to be expected if lithium chloride is a weaker electrolyte than the bromide—some of the reaction products are then present as undissociated lithium chloride. This contradicts the conclusions reached from the results observed in the presence of lithium chloride where in six experiments there was no indication of the reduction in α° required by the assumption of the incomplete dissociation of this salt. Further work appears to be necessary before this discrepancy can be resolved, and in the present investigation only α° values obtained from reaction mixtures containing no added electrolytes were accepted as the mass-law constant in the "85%" solvent.

Discussion

The Rate of Ionisation of Dichlorodiphenylmethane.—The results of this investigation show that the introduction of an α-chloro-group in chlorodiphenylmethane considerably increases the rate of ionisation in aqueous acetone and reduces the Arrhenius activation energy of this process (see Table 5).

Table 5. *The ionisation of chlorodiphenylmethane and chlorodiphenyldimethane in aqueous acetone.*

	Expt. conditions	Ph_2CCl_2	Ph_2CHCl
$10^6k_1^\circ$ (sec.$^{-1}$)	"75%" Aq. acetone, 0°	438	7·61
$10^6k_1^\circ$ (sec.$^{-1}$)	"85%" Aq. acetone, 24·76°	778	21·0
E_A (kcal.)	"85%" Aq. acetone, 0—25°	17·5 *	21·4 †

* This value may be subject to an error of ±1 kcal. as the solvent used at 0° was inadvertently not monitored in the usual manner.

† Hughes, Ingold, and Kohnstam, unpublished work.

These results are in agreement with the predictions of Hughes (*loc. cit.*) who pointed out that the replacement of a hydrogen atom, attached to a C–Cl bond, by chlorine should increase S_N1 reactivity as the expected increase in the electron release to the reaction centre would lower the activation energy of the rate-determining ionisation.

Similar increases in the rate, caused by α-chlorination, have been reported in the ethanolysis of chlorodiphenylmethane (Andrews and Kaeding, *loc. cit.*), in the reaction of benzylidene chloride with aqueous acetone and ethanol (Olivier and Weber, *Rec. Trav. chim.*, 1934, **53**, 869; Hine and Lee, *J. Amer. Chem. Soc.*, 1951, **73**, 22; Evans and Hamann, *Trans. Faraday Soc.*, 1951, **47**, 25), and of allyl chloride in moist formic acid (Vernon, *J.*, 1954, 223). Hine and Lee, and Vernon, also reported a decrease in the activation energy. Evans and Hamann, on the other hand, found an increase in this parameter but a repetition of their work (Bensley and Kohnstam, unpublished work) reverses this conclusion.

It is also of interest to compare these results with the effect of *p*-chloro-substituents on

* The error in I is due only to the overestimate of the ionic strength, and can be shown to be small when compared to the corresponding error in J.

the rate of S_N1 reactions. For example, chloro-*p*-chlorodiphenylmethane undergoes hydrolysis at about one-third of the rate of the parent compound and with a larger activation energy (Ingold, " Structure and Mechanism in Organic Reactions," G. Bell and Sons Ltd., London, 1953, p. 332). In general no compound has yet been reported in which a chlorine atom in the *para*-position relative to the reaction centre acts as an overall electron-donor with respect to hydrogen. It therefore appears that the conjugative electron-release by chlorine can outweigh the attraction due to the inductive effect when the atom is directly attached to the site of reaction. As the *p*-chloro-group acts as an overall attractor in a similar reaction it seems that the demand for electrons is less powerful in that position or, alternatively, that the relay of the conjugative effect to the reaction centre is less efficient.

The Ionic-strength Constant, σ.—The ionic-strength constant, σ, is a measure of the ion-atmosphere stabilisation of the transition state of the rate-determining ionisation. A comparison of our results for chlorodiphenyldimethane with those reported by Hughes, Ingold and their co-workers for chlorodiphenylmethane (*locc. cit.*) shows that this stabilisation is less for the dichloro-compound, $10^8\sigma$ being 1·1 and 1·61, respectively.

σ was evaluated by means of equation (i) which is derived by treating the transition state of ionisation as a dipole with charges $\pm ze$ separated by a distance d, and defining $\sigma = z^2d$. This parameter can therefore be regarded as a measure of the charge separation in the transition state, and it has already been shown that the changes in its value caused by the introduction of *p*-alkyl substituents in chlorodiphenylmethane are consistent with this assumption and with the known polar effects of these groups (*idem, locc. cit.*). The present results show that the introduction of an α-chloro-group in this compound reduces σ, and it therefore appears that the substituent releases electrons towards the reaction centre in the transition state. Such a process will tend to move the effective positive charge out of the benzene rings towards the reaction centre, thus leading to a reduction in the charge separation, relatively to that in the parent compound, as observed. Electron-attraction by this group can be expected to have the converse effect.

The Mass-law Constant, α°.—The carbonium ion, which is formed by the heterolysis of the C–Cl linkage, can undergo one of two reactions; ionic recombination $R^+ + Cl^- \xrightarrow{k_2}$ RCl, or hydrolysis, $R^+ + H_2O \xrightarrow{k_3}$ ROH. The mass-law constant, α°, represents the relative efficiencies of these two processes at zero ionic strength and is defined by $\alpha^\circ = k_2^\circ/k_3^\circ$. The values of this parameter for a number of carbonium ions are compared in Table 6.

TABLE 4. *α° for diphenylmethyl cations in aqueous acetone.*

Cation	Solvent	Temp.	α°
Ph_2CH^+	" 80% ," " 90% "	25, 50°	11·5 *
p-Me·C_6H_4·$CHPh^+$	" 80% "	25	32 *
$(p\text{-Me}\cdot C_6H_4)_2CH^+$	" 80% ," " 85% ," " 90% "	0	74 *
Ph_2CCl^+	" 75% "	0	79
Ph_2CCl^+	" 85% "	25	140
Ph_2CCl^+	" 85% "	0	126

* Hughes, Ingold, *et al.*, *locc. cit.*

It can be seen that the introduction of α-chloro- or *p*-methyl groups in the diphenylmethyl cation considerably increases the mass-law constant. The changes in this parameter due to *p*-alkylation have already been discussed by Hughes, Ingold, and their co-workers (*locc. cit.*) who pointed out that they are a direct consequence of the greater electron-release towards the central carbon atom, which enhances the stability of the carbonium ion. This ion is therefore capable of a longer existence, and thus more liable to penetration of its solvation shell by a chloride ion before this shell collapses to yield the alcohol. On this view the present results again indicate that the α-chloro-substituent acts as an electron-donor relative to hydrogen.

If it can be accepted that electron-release towards the central carbon atom is the principal factor controlling the magnitude of α°, it can also be concluded that the α-chloro-group is capable of at least the same electron-release in the fully developed carbonium ion

as two *p*-methyl groups. In the transition state of the ionisation, where the demand for electrons is less than in the fully developed ion, *p*-alkyl groups are the more efficient electron-donors; the rate of ionisation of chlorodi-*p*-tolylmethane in "85%" aqueous acetone at 0° is about ten times that of dichlorodiphenylmethane, ($10^5k_1^\circ$ = 47 and 5·3 respectively), and it is unlikely that this is entirely due to purely steric factors. It therefore seems that an α-chlorine atom is capable of a greater response to an increased demand for electrons than a *p*-methyl group. As chlorine, unlike the methyl group, possesses unshared electrons this conclusion appears reasonable.

As $\alpha^\circ = k_2^\circ/k_3^\circ$, the change in the value of this parameter with changing temperature may be employed to calculate the difference in the activation energies of the reactions of the carbonium ion with chloride ions and water. The results obtained in the "85%" solvent at 0° and 25° show that for the chlorodiphenylmethyl cation the activation energy for the ionic recombination is 0·9 kcal. greater than for the hydrolysis. This figure cannot be regarded as very accurate as only two experiments were carried out at the lower temperature but it is unlikely to be in error by more than 0·4 kcal. For the same solvent, Hawdon, Hughes, and Ingold (*J.*, 1952, 2499) found that the activation energy for the combination of di-*p*-tolylmethyl ions with azide ions was 4 kcal. greater than for their hydrolysis. Both investigations show that the ionic reaction is associated with the greater activation energy. The energy difference is less in the present case but it must be borne in mind that different cations and anions are involved. There is no reason why the two ionic reactions, or even the two hydrolyses, should have the same activation energy.

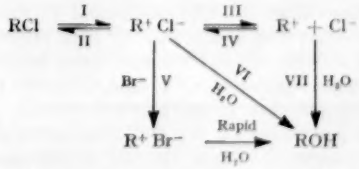
The results quoted in Table 6 show that the mass-law constant of the chlorodiphenylmethyl ion increases as the ionising power of the solvent is reduced, its value at 0° being 79 in the "75%" and 126 in the "85%" solvent. Although this type of behaviour has not been reported before it is consistent with the definition of α° as the ratio of the rates of ionic recombination (k_2°) and hydrolysis of the carbonium ion (k_3°). The passage into the transition state involves a decrease of electric charge for the ionic reaction, and a spreading of charge for the hydrolysis. In general, reactions associated with such changes in charge are accelerated by the use of less powerfully ionising solvents, and this acceleration is greater when a diminution of charge occurs than when the charge is merely rendered more diffuse (Ingold, *op. cit.*, p. 347). A change from "75%" to "85%" aqueous acetone can therefore be expected to produce a greater increase in k_2° than in k_3°, and hence a larger α°.

The Intervention of Ion-pairs.—In the present discussion it has been assumed that the component processes in the S_N1 reactions of the C–Cl linkage are those originally proposed by Hughes and Ingold:

$$RCl \rightleftharpoons R^+ + Cl^- \xrightarrow{H_2O} ROH + H^+ + Cl^-;\ R^+ + Br^- \rightleftharpoons RBr$$

In this scheme only the carbonium ion, R^+, reacts with anions or the solvent.

Recent work on the S_N1 acetolysis of sulphonic esters led Winstein and his co-workers (*Chem. and Ind.*, 1954, 664) to conclude that it is also necessary to take into account the reactions of the "external," or "solvent-separated," ion-pairs, R^+Cl^-, which they regard as intermediate in the formation of the carbonium ion. The application of these views to the present investigation can be represented as follows: *



* Strictly, process V can be expected to be reversible, and the "external" ion-pairs, R^+Br^-, should undergo a series of reactions analogous to those involving R^+Cl^-. It has however been assumed, as by Winstein, that the direct hydrolysis of R^+Y^- can be regarded as instantaneous if RY is hydrolysed much more rapidly than the initial reactant.

The "internal" ion-pair, which does not react with water or other ions, has been omitted from the present scheme.

Qualitatively it is difficult to distinguish between these two views. The Hughes–Ingold scheme requires a retardation of the overall reaction by added chloride ions, but this retardation is not proportional to their concentration as the concomitant increase in the ionic strength reduces their activity coefficient, and also increases the ion-atmosphere stabilisation of the transition state of the ionisation process. These factors also lead to an increase in the hydrolysis rate on the addition of bromide ions. Winstein's scheme predicts similar results but now these are at least partly due to the intervention of the ion-pairs. Equation (i), which is derived from the Hughes–Ingold scheme was found to apply to the present results but this cannot be regarded as conclusive evidence in favour of this scheme. The observed agreement could conceivably arise out of a cancellation of the errors caused by a neglect of the ion-pair reactions and an overestimate of the effect of ionic strength on the activity coefficients of charged species, the most likely error in equation (i) (Hughes, Ingold, *et al.*, *locc. cit.*).

It is however possible to decide which of these schemes applies to the present investigation by considering the results observed in the hydrolysis of dichlorodiphenylmethane at constant ionic strength (cf. Table 2). It was found that the hydrolysis rate was given by the equation

$$10^4(k_1)_0 = C/(1 + D[Cl^-]) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad \text{(iii)}$$

with $C = 4{\cdot}820$ and $D = 36{\cdot}9$, at an ionic strength of 0·0515 in " 75% " aqueous acetone at 0°.

An expression for the hydrolysis rate can be obtained on the basis of Winstein's scheme by applying the stationary-state principle to the carbonium ion and the ion-pair $R^+ Cl^-$. For the range of chloride- and bromide-ion concentrations used in these experiments (cf. Table 2) this expresion only reduces to equation (iii), with $D \sim 35$, if $k_{II} + k_{III} \gg k_{VI} + k_V[Br^-]$. Under these conditions the expression is identical with that which is obtained if only the hydrolysis of the carbonium ion is considered, the contribution due to the hydrolysis of the ion-pairs being negligibly small. The same conclusion can be reached even if process V is considered to be reversible. There is therefore no evidence for the participation of ion-pairs in the hydrolysis of dichlorodiphenylmethane in " 75% " aqueous acetone.

On the other hand, the expression for the hydrolysis rate derived from equation (i) is of the same form as (iii), with $C = 10^4 k_1{}^\circ$ antilog$_{10}$ $(B\sigma\mu)$ and $D = \alpha^\circ$ antilog$_{10}$ $(A\mu^{\frac{1}{2}})$. If the previously determined values of $k_1{}^\circ$ and α° are used, this leads to $C = 4{\cdot}840$ and $D = 38{\cdot}2$, in good agreement with the experimental observations. It therefore appears that the Hughes–Ingold scheme for the component processes in the S_N1 reactions of the C–Cl linkage is applicable to the present investigation.

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Friedel–Crafts Reactions with Methyl m-*Tolyl Ether.*

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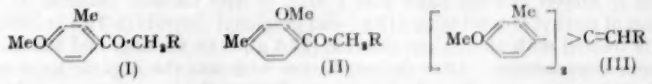
Friedel–Crafts acylation of methyl *m*-tolyl ether has been investigated in detail; it usually gives mixtures of the expected two isomeric ketones, in proportions which vary with the nature of the acylating agent and the experimental conditions. Friedel–Crafts benzylation affords two monobenzyl and one dibenzyl derivative.

Friedel–Crafts acylations have often been performed with methyl *m*-tolyl ether and various acid chlorides (Klages, *Ber.*, 1904, **37**, 3993; von Auwers, Bundesmann, and Wieners, *Annalen*, 1926, **447**, 178; Blau, *ibid.*, 1928, **460**, 93; De Clercq and Buu-Hoï, *Compt. rend.*, 1948, **227**, 1251), but little attention has been paid to the possible formation of isomeric ketones in these reactions. In view of the *ortho*- and *para*-orienting influence of both the methyl and the methoxy-group, such acylations should theoretically lead to mixtures of 4-acyl-3- (I) and 2-acyl-5-methylanisole (II). Buu-Hoï, Royer, and Eckert



recently (*J. Org. Chem.*, 1952, **17**, 1463) found that the reaction with benzoyl chloride in the presence of aluminium chloride yielded both possible ketones. A detailed investigation has now been undertaken of acetylation, propionylation, butyrylation, and phenylacetylation of methyl *m*-tolyl ether, under various experimental conditions. The method for separating the *o*-methoxy-ketones from their *para*-isomers consisted of demethylation to the hydroxy-ketones by pyridine hydrochloride (cf. Buu-Hoï, *Rec. Trav. chim.*, 1949, **68**, 759), and then separation of the *o*- from the *p*-hydroxy-ketones by taking advantage of the lower solubility of the sodium derivatives of the former in concentrated aqueous sodium hydroxide (cf. Coulthard, Marshall, and Pyman, *J.*, 1930, 280).

The results summarized in the Table show that acetylation and butyrylation, with either the acid chloride or the acid anhydride, yielded none or very little of the *o*-methoxy-ketone (II), whereas propionylation, and particularly phenylacetylation, afforded these ketones in considerable amounts. Benzoyl chloride and benzoic anhydride gave the same proportions of *o*- and *p*-ketone. The formation of 1 : 1-di-(4-methoxy-2-methylphenyl)-ethylenes (III) in Friedel–Crafts acylations at high temperature by means of acid chlorides (Xuong and Buu-Hoï, *J.*, 1952, 3741; cf. Gattermann, *Ber.*, 1889, **22**, 1130; Skraup and Nieten, *Ber.*, 1924, **57**, 1300; Mentzer and Xuong, *Compt. rend.*, 1946, **222**, 1004) was observed with acetyl, propionyl, and butyryl chloride. No diarylethylenes were formed when acid anhydrides were used.

Reaction of methyl *m*-tolyl ether with benzyl chloride in the presence of zinc chloride has been shown (Buu-Hoï, Eckert, and Demerseman, *J. Org. Chem.*, 1954, **19**, 726) to be more suitable than the ordinary aluminium chloride-catalyzed Friedel–Crafts reaction for comparing experimental results with the theoretical free-valency indices of the substitution sites. Under the experimental conditions used in the present work, benzylation of methyl *m*-tolyl ether gave 32% of 4-benzyl-3- and 18% of 2-benzyl-5-methylanisole and 29% of 2 : 4-dibenzyl-5-methylanisole. Similar benzylation of *m*-cresol gave 41% of 4-benzyl-3- and 9% of 2-benzyl-5-methylphenol and 25% of 2 : 4-dibenzyl-5-methylphenol. The constitution of the various monobenzyl derivatives was determined by identification with the reduction products of the ketones from Friedel–Crafts benzoylation; that of 2 : 4-dibenzyl-5-methylanisole was determined by its identity with the methylation product of 2 : 4-dibenzyl-3-methylphenol (cf. Huston and Houk, *J. Amer. Chem. Soc.*, 1932, **54**, 1506). From these experiments, it seems that the *para*-position in methyl *m*-tolyl ether is more reactive than the *ortho*-position, a superiority which is less apparent in *m*-cresol itself.

Other experiments included the reaction of phenylmagnesium bromide on 2-methoxy-4-methyl-1-phenacetylbenzene and dehydration of the tertiary alcohol formed, to yield 1-(2-methoxy-4-methylphenyl)-1 : 2-diphenylethylene, and Fischer cyclisation of the phenylhydrazones of the ketones to 2-(2-methoxy-4-methylphenyl)-3-phenylindole. The demethylation of 4-methoxy-2-methylpropiophenone by pyridine hydrochloride and hydrobromic acid is shown in the Table.

Yields (%) on demethylation of 4-hydroxy-2-methylpropiophenone by pyridine hydrochloride and hydrobromic acid (d 1·25; 10 c.c. per g.).

Time (min.)	30	45	55	60	75	90	120	180
C_5H_5N,HCl	30	54	—	64	72	68	63	48
HBr	36	61	69	67	49	26	11	5

4-Methoxy-2- and 2-methoxy-4-methyldibenzyl, prepared by Wolff–Kishner reduction of the corresponding phenylacetophenones, were not cyclized to phenanthrene derivatives by aluminium chloride (Ruzicka and Hösli, *Helv. Chim. Acta*, 1934, **17**, 470; Buu-Hoï and Hoán, *J. Org. Chem.*, 1949, **14**, 1023); only 4-hydroxy-2- and 2-hydroxy-4-methyldibenzyl were formed.

Experimental

Acylations of Methyl m-*Tolyl Ether with* 1 *Mol. of Acid Chloride* (*Method A*).—(*a*) An ice-cooled solution of methyl *m*-tolyl ether (12 g.) and propionyl chloride (9·3 g.) in carbon disulphide (100 c.c.) was treated with aluminium chloride (13·5 g.) with stirring, and the mixture left for 24 hr. at room temperature. After decomposition with ice, the organic layer was collected, washed with 10% aqueous sodium hydroxide (to remove hydroxy-ketones, which were then methylated with methyl sulphate and added to the main portion), then with water, and dried (Na_2SO_4), the solvent was removed, and the residue distilled *in vacuo*. The oil obtained, b. p. 147—158°/15 mm., was kept several days in the refrigerator, and gave crystals (9·2 g.), m. p. 43°, of 4-methoxy-2-methylpropiophenone [*semicarbazone*, prisms, m. p. 209° (from ethanol) (Found : N, 17·8. $C_{12}H_{17}O_2N_3$ requires N, 17·7%)]. The liquid portion was boiled for 40 min. with pyridine hydrochloride (13 g.); after addition of water, the product was taken up in ether, and treated with concentrated aqueous sodium hydroxide. The alkaline solution gave on acidification an oil, which was remethylated with methyl sulphate, to give pure 2-methoxy-4-methylpropiophenone (4·8 g.), b. p. 142—144°/15 mm., n_D^{18} 1·5502 (Mauthner, *J. prakt. Chem.*, 1921, **103**, 395) [*semicarbazone*, m. p. 214° (from ethanol) (Found : N, 17·9%)].

(*b*) With acetyl chloride (7·8 g.), only 4-methoxy-2-methylacetophenone (12·8 g.), b. p. 145—146°/18 mm., n_D^{17} 1·5498 (semicarbazone, m. p. 194°, in agreement with Auwers *et al.*, *loc. cit.*), was obtained.

(*c*) With *n*-butyryl chloride (10·6 g.), the oil obtained (14·6 g.), b. p. 158—170°/16 mm., was demethylated to a portion (0·3 g.), whose sodium derivative was insoluble in concentrated aqueous sodium hydroxide; it gave 2-methoxy-4-methyl-*n*-butyrophenone semicarbazone, m. p. 192°. The soluble product was 4-hydroxy-2-methyl-*n*-butyrophenone, m. p. 98° (from ethanol–water). Remethylation of this ketone gave pure 4-methoxy-2-methyl-*n*-butyrophenone, b. p. 161—163°/15 mm., n_D^{21} 1·5376 [*semicarbazone*, prisms, m. p. 182°, from ethanol (Found : N, 16·7. $C_{13}H_{19}O_2N_3$ requires N, 16·7%)].

(*d*) With phenylacetyl chloride (15·5 g.), an oil, b. p. 234—236°/15 mm., was obtained, which was diluted with light petroleum and kept for several days in the refrigerator. 4-Methoxy-2-methyl-1-phenylacetylbenzene (9·4 g.) formed prisms, m. p. 73°, from ethanol (cf. Blau, *Monatsh.*, 1905, **26**, 1149) [*semicarbazone*, prisms, m. p. 165° (from ethanol–water) (Found : C, 65·7; H, 6·5; N, 14·2. $C_{17}H_{19}O_2N_3$ requires C, 65·6; H, 6·4; N, 14·1%)]. The liquid portion, purified *via* its demethylation product, gave 2-*methoxy*-4-*methyl*-1-*phenylacetylbenzene* (8·7 g.), a pale yellow oil, b. p. 221—222°/15 mm., n_D^{21} 1·5870 (Found : C, 80·3; H, 6·2. $C_{16}H_{16}O_2$ requires C, 80·0; H, 6·1%) [*semicarbazone*, prisms, m. p. 198° (from ethanol–water) (Found : N, 14·1%)]. In this and the preceding cases only traces of diarylethylene were detected.

(*e*) Benzoyl chloride (14·2 g.) gave a ketone mixture (17·4 g.), which was converted into 4-methoxy-2-methylbenzophenone (Buu-Hoï, Royer, and Eckert, *loc. cit.*), and 2-*methoxy*-4-*methylbenzophenone*, a pale yellow oil, b. p. 204—205°/16 mm., n_D^{19} 1·6105 (Found : C, 79·5; H, 6·3. $C_{15}H_{14}O_2$ requires C, 79·6; H, 6·2%) [*semicarbazone*, prisms, m. p. 182° (from ethanol–water) (Found : N, 14·8. $C_{16}H_{17}O_2N_3$ requires N, 14·8%)].

Acylation of Methyl m-*Tolyl Ether with* 0·5 *Mol. of Acid Chloride* (*Method B*).—To a solution

of methyl *m*-tolyl ether (2 mol.) and the acid chloride (1 mol.), aluminium chloride (1·5 mol.) was added in small portions with stirring. The mixture was kept for 1 hr. at 70°, then for 24 hr. at room temperature. After treatment with ice, the product was dissolved in ether and worked up as above; the *o*-methoxy-ketone was obtained in the lower-boiling portion, and the higher-boiling residue consisted mainly of the 1 : 1-diarylethylene. **1 : 1-*Di*-(4-*methoxy*-2-*methylphenyl*)*ethylene*,** b. p. 205—210°/17 mm., crystallized as leaflets, m. p. 133°, from ethanol (Found: C, 81·6; H, 7·4. $C_{18}H_{20}O_2$ requires C, 81·3; H, 7·2%), and **1 : 1-*di*-(4-*methoxy*-2-*methylphenyl*)*butene*,** b. p. 162—165°/1 mm., as leaflets, m. p. 82°, from methanol (Found: C, 78·3; H, 7·7. $C_{20}H_{24}O_2$ requires C, 78·1; H, 7·8%). Both compounds gave a red halochromy with sulphuric acid.

Acylation of Methyl m-*Tolyl Ether with Acid Anhydride* (*Method C*).—The technique used was that of Noller and Adams (*J. Amer. Chem. Soc.*, 1924, **46**, 1892). The yields recorded in the Table were reproduced to within 2% in at least two experiments for each case.

Yields (%) of ketones and 1 : 1-*diarylethylenes in Friedel–Crafts acylation of methyl* m-*tolyl ether.*

		Method A	Method B	Method C
Acetylation	*o*-Methoxy-ketone	Nil	Nil	Nil
	p-Methoxy-ketone	78	66	82
	Diarylethylene	Trace	22	Nil
Propionylation	*o*-Methoxy-ketone	27	Nil	32
	p-Methoxy-ketone	52	58	52
	Diarylethylene	Trace	25	Nil
Butyrylation	*o*-Methoxy-ketone	Trace	Nil	5
	p-Methoxy-ketone	70	52	78
	Diarylethylene	Nil	19	Nil
Phenacetylation	*o*-Methoxy-ketone	39	Nil	—
	p-Methoxy-ketone	36	39	—
	Diarylethylene	3	34	—
Benzoylation	*o*-Methoxy-ketone	18	Nil	21
	p-Methoxy-ketone	59	72	62

4-*Methoxy*-2-*methyldibenzyl*.—A solution of 4-methoxy-2-methyl-1-phenylacetylbenzene (22·6 g.) and 90% hydrazine hydrate (8 g.) in diethylene glycol (200 c.c.) was heated for 15 min.; potassium hydroxide (9 g.) was added, and the mixture was refluxed with removal of water for 3 hr. After cooling, dilute hydrochloric acid was added, and the product taken up in benzene. The benzene layer was washed with 10% aqueous sodium hydroxide (solution A), then with water, and dried (Na_2SO_4). The residue from evaporation of benzene gave on fractionation *in vacuo*, pure **4-*methoxy*-2-*methyldibenzyl*** (18 g.), b. p. 214—216°/16 mm., needles, m. p. 71° (from methanol) (Found: C, 84·7; H, 7·9. $C_{16}H_{18}O$ requires C, 84·9; H, 7·9%). The substance described by Hill and Short (*J.*, 1935, 1123) as an oil, b. p. 180—190°/10 mm., was probably a mixture of isomers. Acidification of the alkaline solution afforded **4-*hydroxy*-2-*methyldibenzyl*** (1·3 g.), prisms, m. p. 137—138° (from methanol) (Found: C, 84·7; H, 7·5. $C_{15}H_{16}O$ requires C, 84·9; H, 7·5%).

2-*Methoxy*-4-*methyldibenzyl*.—Prepared as above from 2-methoxy-4-methyl-1-phenylacetylbenzene, this *compound* (9 g.) was a colourless oil, b. p. 187—189°/16 mm., n_D^{19} 1·5770 (Found: C, 85·1; H, 7·9%). **2-*Hydroxy*-4-*methyldibenzyl*** (0·6 g.) was an oil, b. p. 226—230°/16 mm., n_D^{23} 1·5842 (Found: C, 85·1; H, 7·4%).

1-(2-*Methoxy*-4-*methylphenyl*)-1 : 2-*diphenylethylene*.—2-Methoxy-4-methyl-1-phenylacetylbenzene similarly gave **1-(2-*methoxy*-4-*methylphenyl*)-1 : 2-*diphenylethan*-1-ol** (4·4 g.), prisms, m. p. 140° (from methanol) (Found: C, 82·9; H, 6·8. $C_{22}H_{21}O_2$ requires C, 83·2; H, 6·6%); dehydration with formic acid yielded the *ethylene*, b. p. 245°/17 mm., prisms, m. p. 77° (from methanol) (Found: C, 87·8; H, 6·1%).

2-(4-*Methoxy*-2-*methylphenyl*)-3-*phenylindole*.—The crude phenylhydrazone of 4-methoxy-2-methyl-1-phenacetylbenzene was cyclized with acetic acid saturated with hydrogen chloride (cf. Buu-Hoï, *J.*, 1949, 2882), to give **2-(4-*methoxy*-2-*methylphenyl*)-3-*phenylindole***, b. p. 305—310°/15 mm., leaflets, m. p. 176° (from ethanol) (Found: C, 84·3; H, 6·1. $C_{22}H_{19}ON$ requires C, 84·3; H, 6·1%). **2-(2-*Methoxy*-4-*methylphenyl*)-3-*phenylindole***, similarly prepared from 2-methoxy-4-methyl-1-phenylacetylbenzene, boiled at 300—302°/15 mm., and crystallized as leaflets, m. p. 138°, from ethanol (Found: C, 83·6; H, 6·2%).

Benzylation of Methyl m-*Tolyl Ether*.—A solution of methyl *m*-tolyl ether (61 g.) and benzyl chloride (70 g.) in dry chloroform (400 c.c.) was refluxed with freshly fused, finely powdered zinc

chloride (30 g.) for 15 hr. The chloroform layer which was formed on treatment with water was washed with water, then dried (Na_2SO_4), and the residue on evaporation of the solvent was fractionated *in vacuo*. The fraction of b. p. 175—195°/15 mm. (56 g.) partly solidified after prolonged storage in the refrigerator. The solid gave, on recrystallization from light petroleum, *4-benzyl-3-methylanisole* (32%), prisms, m. p. 43° (Found: C, 85·1; H, 7·4. $C_{15}H_{16}O$ requires C, 84·9; H, 7·5%), identical with the Wolff–Kishner reduction product of 4-methoxy-2-methylbenzophenone; the product described by Stadnikov and Baryscheva (*Ber.*, 1928, **61**, 1999) as an oil, b. p. 181—187°/20 mm., n_D^{18} 1·5767, was probably a mixture. After repeated fractional crystallization, the liquid portion was redistilled, giving *2-benzyl-5-methylanisole* (18%), b. p. 179°/15 mm., n_D^{18} 1·5864 (Found: C, 85·2; H, 7·4%), identical with the Wolff–Kishner reduction product of 2-methoxy-4-methylbenzophenone. The portion of b. p. 240—255°/15 mm. (28·5 g.) was 2 : 4-*dibenzyl-5-methylanisole*, which crystallized from light petroleum as prisms, m. p. 70° (Found: C, 87·3; H, 7·1. $C_{22}H_{22}O$ requires C, 87·4; H, 7·3%), and was demethylated by pyridine hydrochloride to 2 : 4-dibenzyl-5-methylphenol, m. p. 106°.

Benzylation of m-*Cresol.*—A solution of *m*-cresol (55 g.) and benzyl chloride (70 g.) in chloroform (400 c.c.) was refluxed for 10 hr. with zinc chloride (30 g.), and the mixture worked up as above. Repeated fractionation *in vacuo* gave a 9% yield of 2-benzyl-5-methylphenol, b. p. 123—127°/1 mm., m. p. 47° (from light petroleum), a 41% yield of 4-benzyl-3-methylphenol, b. p. 147—150°/1 mm., m. p. 93·5° (from ligroin), and a 25% yield of 2 : 4-dibenzyl-5-methylphenol, m. p. 106° (from benzene), in accord with Huston and Houk (*loc. cit.*).

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Studies in the Steroid Group. Part LXX. Reactions at $C_{(11)}$ in 9β-Steroids.*

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[Reprint Order No. 6414.]

The 11α-alcohol is the only epimer produced by the reduction under various conditions of an 11-ketone with an adjacent 9β-configuration. In hydrogenation and lithium aluminium hydride reduction the reactions provide further examples of the greater accessibility of the β-face of 9β-steroids (earlier examples, *J.*, 1953, 2921; *J.*, 1954, 728). Δ^{11}-Compounds are described in the 9α- and the 9β-series; in the latter, hydrogenation affords a saturated 9β-stanol (9β-ergostan-3β-ol). The possible conformations of 9β-steroids are discussed.

The boron trifluoride-catalysed isomerisation of Δ^7-9α : 11α-epoxides of the steroid series to Δ^7-11-ketones [*e.g.*, (I)] with an "unnatural" 9β-configuration has been described in detail (Bladon, Henbest, Jones, Lovell, Wood, and Woods; Elks, Evans, Hathway, Oughton, and Thomas, *J.*, 1953, 2921; cf. also Heusler and Wettstein, *Helv. Chim. Acta*, 1953, **36**, 398). In contrast to Δ^7-steroids with a 9α-configuration, Δ^7-bonds in 9β-compounds were found to be readily hydrogenated, 7 : 8β-dihydro-products [*e.g.*, (II)] being formed stereospecifically. Both ketones (I) and (II) could be isomerised to more stable 9α-compounds of the natural series.

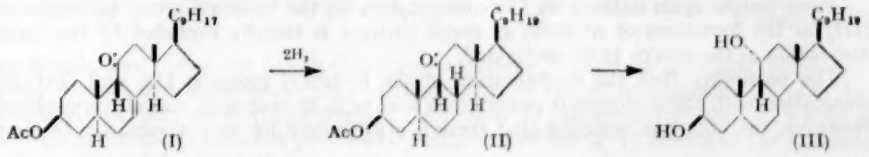
As part of a study of the chemistry of steroid compounds with unusual stereochemical features, reduction of 11-ketones (II) of the 9β-series has been investigated. With lithium aluminium hydride or lithium–ammonia–ethanol, the ketone (II) gave the *same* 3 : 11-diol in high yield, none of the epimeric 11-alcohol being detected by chromatographic techniques. [Sodium–ethanol reduction was less satisfactory, some epimerisation occurring at $C_{(9)}$ before reduction.] These results may be contrasted with the position in the 9α-series where lithium aluminium hydride gives (axial) 11β-alcohols and metal–alcohol reduction affords (equatorial) 11α-alcohols, both formed in high yields.

Hydrogenation of ketones in acidic solution often affords the less stable isomer (axial in

* Part LXIX, *J.*, 1955, 2477.

*cyclo*hexane series), and attempts were thus made to prepare the epimeric 11-alcohol from the ketone (II). However, in only one experiment was an 11-alcohol isolated, and this proved to be identical with that already encountered; if any of the epimer was produced in this reaction the yield must have been very small. Alkaline epimerisation of the new 11-alcohol was not studied as the reaction would have to proceed *via* the 9β-11-ketone (II) under conditions sufficiently alkaline to cause epimerisation of this intermediate to the 9α-11-ketone.

The new 3 : 11-diol of the 9β-series was converted into a 3β-monoacetate by acetylation at 20°, and into a diacetate by acetylation at 90° (acetic anhydride–pyridine). The reactivity of the 11-hydroxyl group towards acylation is thus intermediate between those of 11α- and 11β-hydroxy-groups in the 9α-series. The 11-hydroxyl group in the new diol



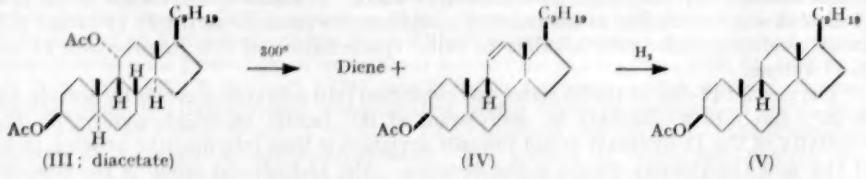
has been assigned an α-configuration (III) on evidence from (*a*) optical rotations and (*b*) olefin formation under various conditions. Klyne and Stokes (*J.*, 1954, 1979) have shown that the optical rotation contributions of hydroxyl (and derived ester) groups in alicyclic compounds containing the grouping $\begin{matrix}C\\C\end{matrix}\!>\!CH\cdot CH(OR)\cdot CH_2\cdot$ may be correlated with the configuration of the alcohol. From our data presented in the Table it can be seen that the negative contribution of the 11-hydroxyl group in our alcohol (III), and the much larger negative contribution of the 11-acetate, correspond to α-configurations.

	$[M]_D$ Values					Δ Values			
	C_{11}-Substituents					α-Substituents		β-Substituents	
Parent compound	H	α-OH	α-OAc	β-OH	β-OAc	ΔOH	ΔOAc	ΔOH	ΔOAc
Ergostanol	+64°	−9°	—	+118°	+208°	−73°	—	+58°	+144°
Ergostanyl acetate ...	+27	—	−105°	+115	+155	—	−132°	+88	+128
9β-Ergostanol	+160	+150	—	—	—	−10	—	—	—
9β-Ergostanyl acetate	+121	+115	−8	—	—	−6	−129	—	—

Dehydration of the 3β-monoacetate of (III) by phosphorus oxychloride and pyridine afforded 3β-acetoxyergost-9-ene, but since the 11-epimer was not available, and since this Δ^9-compound is formed from both the 11α- and the 11β-alcohol in the 9α-series (Crawshaw, Henbest, and Jones, *J.*, 1954, 731), the reaction provides no configurational evidence. Treatment of the 3β-monoacetate with hydrochloric acid in acetic acid also readily afforded the Δ^9-olefin—this observation could be taken as indicating a diaxial arrangement of eliminated groups, as Bernstein, Lenhard, and Williams (*J. Org. Chem.*, 1954, **19**, 41) observed (and we have confirmed in the ergostane series) that axial 11β-alcohols in the 9α-series were dehydrated by this reagent whereas the 11α-hydroxy-compounds were acetylated. On the other hand, an axial configuration appears unlikely in view of the formation of the alcohol by metal–alcohol reduction (but see further discussion below).

Thermal decomposition of esters to olefins and acids is known to proceed with *cis*-elimination in *cyclo*hexane compounds. Pyrolysis of the 3 : 11-diacetate of (III) at 300° gave a mixture of diene, acetoxy-olefin, and starting material, readily separated by chromatography. The acetoxy-olefin fraction consisted mainly of 3β-acetoxy-9β-ergost-11-ene (IV). Comparative experiments in the 9α-series with both the 11α- and the 11β-acetate gave similar yields of diene and acetoxy-olefin fractions. Thus the 3β : 11β-diacetate (VI) yielded the Δ^{11}-compound, and the 3β : 11α-diacetate gave the Δ^9-olefin as the major components of the acetoxy-olefin fractions. The structures of the two Δ^{11}-compounds (IV) and (VII) were established by the strong absorption bands in the infrared spectrum in the 700—800 cm.$^{-1}$ region (Henbest, Meakins, and Wood, *J.*, 1954,

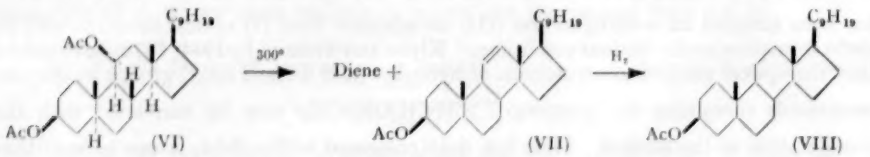
800) and by their further reactions (see below). If $C_{(10)}$ is regarded as an allylic substituent to ring C, the relative rotations of the olefins (IV) and (VII) (latter more positive) fitted the relationship developed for allylic systems by Mills (*J.*, 1952, 4976).



(III; diacetate) (IV) (V)

These results again indicate an 11α-configuration for the hydroxyl group in compound (III) as the formation of Δ^9-olefin as major product is thereby excluded by the *trans*-disposition of the groups to be eliminated.

The possibility that the configuration of the hydroxyl group is 11β, and that *cis*-elimination with 12β-hydrogen is preferred to that with 9β-hydrogen, was also considered. However, the literature indicates that there is a preference for such elimination to occur



(VI) (VII) (VIII)

towards the more substituted position (cf. Barton, *J.*, 1949, 2174; Barton and Rosenfelder, *J.*, 1949, 2459; *J.*, 1951, 1048). Further examples are the preferential formation of $\Delta^{1(9)}$-octalin from *trans*-α-decalol (m. p. 63°) (Hückel and Naab, *Annalen*, **1933**, **502**, 136), and the Δ^9-olefin from the 11α-acetate in the 9α-series (above).

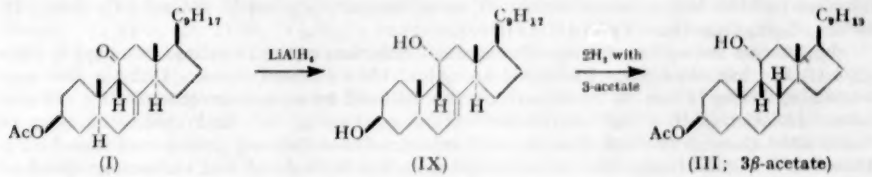
In so far as the relative stabilities of the olefinic products influence the direction of elimination, Δ^9-steroids appear, from the evidence of their invariant formation from 11-oxygenated compounds under " ionic " conditions, to be more stable than Δ^{11}-compounds (cf. Crawshaw, Henbest, and Jones, *loc. cit.*). This may be related in part to the circumstance that Δ^9-bonds lie opposite to the *trans*-ring fusion of rings C and D (cf. stability of Δ^2-compounds in *trans*-A/B series).

Hydrogenation of the Δ^{11}-compounds (IV) and (VII) afforded derivatives of 9β-ergostanol (V) and ergostanol (VIII) respectively. Oxidation of 9β-ergostanol gave the 3-ketone, which readily gave a dinitrophenylhydrazone (11-ketones of the 9β-series do not). The position of the carbonyl stretching frequency in the infrared (1710 $cm.^{-1}$) also indicated the structure of a 3-ketone (the more heavily adjacently alkylated 11-ketones of the 9α- and 9β-series exhibit bands at frequencies just less than 1700 $cm.^{-1}$). These reactions exclude the possibility that the acetoxy-olefin was produced by elimination in ring A; the final ketone would then have been 9β-ergostan-11-one.

Actually the Δ^{11}-compounds were accompanied by smaller amounts of Δ^9-isomers and *vice versa* in these pyrolytic experiments. The proportions of each could be estimated from the intensities of the C–H bending frequencies in the infrared spectrum (see Experimental section). The preferential formation of ring-C rather than ring-A olefins deserves comment, since it might be expected that the former would be more strained, involving flattening of a more rigid part of the molecule. Infrared measurements at room temperature support this suggestion (Henbest, Meakins, and Wood, *loc. cit.*), although of course at the higher temperatures of the elimination reaction the energy relations may be modified. A factor favouring elimination from $C_{(11)}$ could be the greater relief of steric compression in this more crowded part of the molecule.

Reduction of the $\Delta^{7:22}$-11-ketone of the 9β-series (I) by lithium aluminium hydride yielded only the 11α-alcohol (IX), hydrogenated to the saturated alcohol obtained previously. Heusler and Wettstein (*loc. cit.*) have also described this particular reduction.

Upon acetylation of the reaction product they obtained a mono- and a di-acetate which, by analogy with the known relative case of acetylation in the 9α-*series*, were designated as 3β-acetoxy-11β-hydroxy- and 3β : 11α-diacetoxy-compounds respectively. Repetition and further examination of the acetylation has shown that the monacetate is actually the 3-acetate of the 3β : 11α-diol (IX), and the diacetate is the corresponding diester. As in



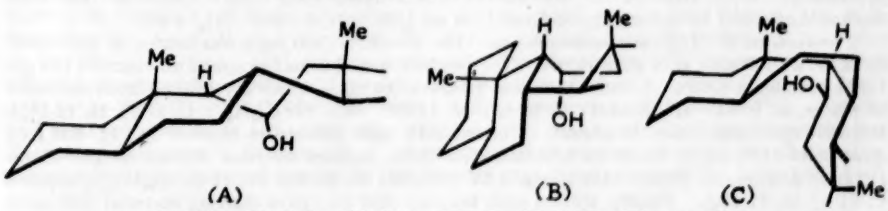
(I) (IX) (III; 3β-acetate)

the 9β-saturated series, the 11α-hydroxy-group in these Δ^7-compounds is acetylated only slowly at 20°, but rapidly at 100°. Dehydration of the 3β-monoacetate of (IX) by phosphorus oxychloride–pyridine afforded the 7 : 9-diene; this was also formed by similar dehydration of the 11β-alcohol produced by reduction of the Δ^7-11-ketone of the 9α-series by lithium aluminium hydride.

Conformation of 9β-*Steroids.*—Inspection of models of a saturated 9β-steroid shows that either ring B or ring C must assume a boat conformation (another form in which B and C are both boat will not be considered). Three models can be constructed (see Figure) and these are readily interconvertible by suitable concerted twisting of bonds (as with the boat forms of *cyclo*hexane and with the two equivalent forms of *cis*-decalin). Conformational analysis of the three structures (Barton, *Experientia*, 1950, **6**, 316; Johnson, *J. Amer. Chem. Soc.*, 1953, **75**, 1498) in an attempt to predict the form of greatest stability showed that no appreciable energy differences would be expected. Thus it seems unlikely that any one rigid conformation would predominate during reactions in solution, but rather that the molecule would adopt the conformation which would give the best transition state or complex for the particular reaction.

Reduction of the 11-ketone by approach of lithium aluminium hydride or hydrogenation catalyst to the β-face of the molecule may involve conformation C, where the angular methyl groups normally hindering β-approach are spread far apart, and ring A shields the 11-ketone from α-approach. In this conformation, the resulting 11α-hydroxyl

Conformations of 9β-*ergostane compounds.*



(A) (B) (C)

A *and* B : 11α-*hydroxyl is boat-axial.* C : 11α-*hydroxyl is equatorial.*

group is also equatorial, in accord with its formation by metal–alcohol reduction. If interconversion of the three conformations is assumed, the ready acid-catalysed dehydration of the 11α-hydroxyl function described above may take place by a normal diaxial elimination from conformation A or B.

Experimental

General experimental directions are as given in Part LXI, *J.*, 1953, 2916.

Reduction of 3β-*Acetoxy*-9β-*ergostan*-11-*one* (II).—(a) *Lithium aluminium hydride.* A solution of the ketone (1 g.) in dry ether (250 c.c.) was heated under reflux for 1 hr. with the

hydride (250 mg.). The product isolated in the usual way was crystallised from methanol, to give 9β-*ergostane*-3β : 11α-*diol* as needles, m. p. 201—205°, $[\alpha]_D$ +45° (Found: C, 80·35; H, 12·1. $C_{28}H_{50}O_2$ requires C, 80·35; H, 12·05%). Acetic anhydride and pyridine at 20° overnight converted the diol in high yield into 3β-*acetoxy*-9β-*ergostan*-11α-*ol* (needles from nitromethane), m. p. 143·5—144·5°, $[\alpha]_D$ +25° (Found: C, 78·15; H, 11·3. $C_{30}H_{52}O_3$ requires C, 78·3; H, 11·4%). Similar acetylation at 100° for 6 hr. afforded 3β : 11α-*diacetoxy*-9β-*ergostane* (needles from aqueous methanol), m. p. 94—95°, $[\alpha]_D$ −1·5° (Found: C, 76·25; H, 10·95. $C_{32}H_{54}O_4$ requires C, 76·4; H, 10·85%).

(b) *Lithium and methanol in liquid ammonia.* Solutions of the 11-ketone (500 mg.) in ether (20 c.c.) and methanol (6 c.c.) in liquid ammonia (150 c.c.) were mixed. Lithium (500 mg.) was added during 15 min. to the stirred solution, followed by ammonium chloride (1 g.) 15 min. later. Isolation with ether, acetylation of the product at 20°, and chromatography on deactivated alumina afforded 3β-acetoxy-9β-ergostan-11α-ol (400 mg.), m. p. and mixed m. p. 138—141°. Alternatively, the reduction product was hydrolysed and chromatographed on alumina (100 g.). The product was homogeneous, all being eluted with benzene–ether (4 : 1) to give the 3β : 11α-diol (450 mg.), m. p. and mixed m. p. 206—207°.

(c) *Hydrogenation in acetic acid.* The ketone (1·5 g.) in acetic acid (400 c.c.) was stirred with Adams catalyst (500 mg.) at 50° in an autoclave containing hydrogen (75 atm.) for 4 hr. The product was chromatographed on alumina (150 g.). Elution with light petroleum–benzene (1 : 1) (1·5 l.) gave starting material (1·2 g.), which crystallised from acetone, then having m. p. 155—156°. Elution with ether–methanol (100 : 1) afforded a gum (300 mg.), which on crystallisation from methanol gave 3β-acetoxy-9β-ergostan-11α-ol, m. p. and mixed m. p. 140—143°, $[\alpha]_D$ +29°. Attempted hydrogenation at atmospheric pressure only gave starting material.

(d) *Hydrogenation in acetic acid and hydrochloric acid.* A solution of the 11-ketone (500 mg.) in acetic acid (50 c.c.) containing hydrochloric acid (2 drops) was shaken in hydrogen until gas absorption ceased (30 min.). Chromatography of the product afforded 3β-acetoxyergostane (270 mg.), m. p. 143—147°, $[\alpha]_D$ +9°, and starting material (220 mg.), m. p. 155—156°.

Dehydration of 3β-*Acetoxyergostan*-11β-*ol.*—The steroid (150 mg.) in acetic acid (10 c.c.) and concentrated hydrochloric acid (1 c.c.) was heated under reflux for 30 min. Isolation with ether and crystallisation from methanol afforded a good yield of 3β-acetoxyergost-9-ene, m. p. 120—130°, $[\alpha]_D$ +15°.

Similar treatment of ergostane-3β : 11α-diol afforded 3β : 11α-diacetoxyergostane, m. p. and mixed m. p. 114—117°.

Dehydration of 3β-*Acetoxy*-9β-*ergostan*-11α-*ol.*—(*a*) A solution of the steroid (280 mg.) in acetic acid (20 c.c.) and concentrated hydrochloric acid (2 c.c.) was heated under reflux for 30 min. Crystallisation of the product from methanol gave 3β-acetoxyergost-9-ene (200 mg.) as fine needles, m. p. and mixed m. p. 126—129°, $[\alpha]_D$ +15°.

(*b*) Phosphorus oxychloride (0·75 c.c.) was added to a solution of the steroid (150 mg.) in pyridine (4 c.c.). After 12 hr., the steroid was isolated with ether. Crystallisation from methanol afforded 3β-acetoxyergost-9-ene (100 mg.), m. p. 131—132°, $[\alpha]_D$ +18°.

Pyrolysis of 3β : 11β-*Diacetoxyergostane.*—The diacetate (500 mg.) was heated at 280—300° for 2 hr. at 200 mm. in a glass retort. The product was chromatographed on alumina (50 g.). Light petroleum (250 c.c.) eluted the diene mixture (40 mg.), which crystallised from methanol as plates, m. p. 84—91° (Found: C, 87·85; H, 11·85. Calc. for $C_{28}H_{46}$: C, 87·7; H, 12·1%). Infrared spectrum: acetate absent. Elution with light petroleum–benzene (1 : 1; 500 c.c.) gave solid (150 mg.), which on crystallisation from acetone afforded 3β-*acetoxyergost*-11-*ene* (VII) as needles, m. p. 129—132°, $[\alpha]_D$ +25° (Found: C, 81·55; H, 11·3. $C_{30}H_{50}O_2$ requires C, 81·4; H, 11·4%). Finally, elution with benzene (250 c.c.) gave starting material (205 mg.). Hydrogenation of 3β-acetoxyergost-11-ene in acetic acid (Adams catalyst) afforded 3β-acetoxyergostane, m. p. and mixed m. p. 146—147°, $[\alpha]_D$ +6°.

The following compounds were also prepared during this study. Lithium aluminium hydride reduction of 3β-acetoxyergostan-11-one gave *ergostane*-3β : 11β-*diol* (plates from acetone), m. p. 175—176°, $[\alpha]_D$ +28° (Found, on sublimed sample: C, 80·2; H, 12·0. $C_{28}H_{50}O_2$ requires C, 80·35; H, 12·05%). Hydrolysis of 3β : 11β-diacetoxyergostane with potassium hydroxide in ethanol at 20° yielded 11β-*acetoxyergostan*-3β-*ol* (fine needles from methanol), m. p. 140—141°, $[\alpha]_D$ +46° (Found: C, 78·3; H, 11·45. $C_{30}H_{52}O_3$ requires C, 78·2; H, 11·4%). Oxidation of this compound with chromic acid in acetone (cf. *J.*, 1951, 2402) afforded 11β-*acetoxyergostan*-3-*one* (needles from acetone), m. p. 136—138°, $[\alpha]_D$ +50° (Found: C, 78·55; H, 11·2. $C_{30}H_{50}O_3$ requires C, 78·55; H, 11·0%).

Pyrolysis of 3β : 11α-*Diacetoxyergostane.*—The diacetate was pyrolysed as described above.

Chromatography gave diene (30 mg.), a mixture of acetoxy-olefins (130 mg.), and starting material (250 mg.). The acetoxy-olefin fraction had m. p. 120—122°; it contained 70% of the Δ^9-compound (see below for infrared data) but this could not be obtained pure by crystallisation, owing to the smaller solubility of the Δ^{11}-isomer.

Pyrolysis of 3β : 11α-*Diacetoxy*-9β-*ergostane*.—Pyrolysis as above gave diene (30 mg.), acetoxy-olefin fraction (210 mg.), and starting material. Crystallisation of the olefin fraction from methanol yielded 3β-*acetoxy*-9β-*ergost*-11-*ene* (IV) as plates, m. p. 114—116°, $[\alpha]_D$ −65° (Found : C, 81·5; H, 11·45. $C_{30}H_{50}O_2$ requires C, 81·4; H, 11·4%). Hydrogenation of the olefin in acetic acid (Adams catalyst) afforded 3β-*acetoxy*-9β-*ergostane* (V) (plates from methanol), m. p. 145—148°, $[\alpha]_D$ +48° (Found : C, 81·2; H, 11·8. $C_{30}H_{52}O_2$ requires C, 81·0; H, 11·8%). Alkaline hydrolysis gave 9β-*ergostan*-3β-*ol* (plates from acetone), m. p. 147—148°, $[\alpha]_D$ +40° (Found : C, 83·25; H, 12·7. $C_{28}H_{50}O$ requires C, 83·5; H, 12·5%). Oxidation with chromic acid in acetone yielded 9β-*ergostan*-3-*one* (plates from acetone–methanol), m. p. 150—151°, $[\alpha]_D$ +65° (Found : C, 83·9; H, 11·95. $C_{28}H_{48}O$ requires C, 83·95; H, 12·1%). This ketone gave a 2 : 4-*dinitrophenylhydrazone* (needles from ethyl acetate–methanol), m. p. 223—226° (Found : C, 70·25; H, 9·3; N, 9·6. $C_{34}H_{52}O_4N_4$ requires C, 70·3; H, 9·0; N, 9·65%).

Analysis of the Acetoxy-olefin Fractions from the Pyrolyses.—Olefinic C–H out-of-plane bending frequencies were determined in CS_2 solution with a sodium chloride prism as follows : 3β-acetoxyergost-11-ene, 755 and 722 cm.$^{-1}$; 3β-acetoxy-9β-ergost-11-ene, 764 and 725 cm.$^{-1}$; and 3β-acetoxyergost-9-ene, 824 cm.$^{-1}$. With the Δ^{11}-compounds, the bands at 722 and 725 cm.$^{-1}$ respectively were used as reference bands for analysis of the pyrolysis mixtures. The ε values were computed as before (*J.*, 1954, 800).

	Peak frequency	ε	Δ^9 (%)	Δ^{11} (%)
3β-Acetoxyergost-11-ene	722	60	—	100
3β-Acetoxy-9β-ergost-11-ene	725	56	—	100
3β-Acetoxyergost-9-ene	824	66	100	—
Pyrolysis product from 3β : 11α-diacetoxyergostane	722	22	—	35
	824	47	70	—
Pyrolysis product from 3β : 11β-diacetoxyergostane	722	38	—	65
	824	16	25	—
Pyrolysis product from 3β : 11α-diacetoxy-9β-ergostane	725	37	—	65
	824	25	40	—

Preparation and Reactions of 9β-*Ergosta*-7 : 22-*diene*-3β : 11α-*diol* (IX).—Solutions of 3β-acetoxy-9β-ergosta-7 : 22-dien-11-one (3 g.) in dry ether (100 c.c.) and lithium aluminium hydride (15 c.c. of 0·5M-solution) were mixed and heated under reflux for 1 hr. After isolation with ether, the product was acetylated with acetic anhydride (24 c.c.) and pyridine (60 c.c.) at 20° for 22 hr. This product was chromatographed on deactivated alumina (150 g.). Light petroleum (400 c.c.) eluted material, m. p. 167—173°; further washing with the same solvent (1250 c.c.) gave an oil (800 mg.) which on crystallisation from methanol afforded 3β : 11α-diacetoxy-9β-ergosta-7 : 22-diene as needles, m. p. 151—153°, $[\alpha]_D$ −139° (Found : C, 76·9; H, 9·9. Calc. for $C_{32}H_{50}O_4$: C, 77·05; H, 10·1%). Heusler and Wettstein (*loc. cit.*) give m. p. 145·5—147°, $[\alpha]_D$ −158°, for this compound. Further elution with benzene–ether (9 : 1) afforded 3β-*acetoxy*-9β-*ergosta*-7 : 22-*dien*-11α-*ol* (1·6 g.) (needles from methanol), m. p. 169—173°, $[\alpha]_D$ −114° (Found : C, 79·0; H, 10·55. $C_{30}H_{48}O_3$ requires C, 78·9; H, 10·6%). Heusler and Wettstein give m. p. 166—169°, $[\alpha]_D$ −111°, for this compound which they suggested was 3β-acetoxy-9β-ergosta-7 : 22-dien-11β-ol. Acetylation of 3β-acetoxy-9β-ergosta-7 : 22-dien-11α-ol with acetic anhydride and pyridine at 100° for 6 hr. gave the above diacetate, m. p. 147—150°, $[\alpha]_D$ −140°.

Hydrogenation of 3β-acetoxy-9β-ergosta-7 : 22-dien-11α-ol in acetic acid (Adams catalyst) afforded 3β-acetoxy-9β-ergostan-11α-ol, m. p. 139—142°, $[\alpha]_D$ +23°.

Dehydration of 3β-acetoxy-9β-ergosta-7 : 22-dien-11α-ol with phosphorus oxychloride in pyridine at 20° for 12 hr. gave 3β-acetoxyergosta-7 : 9 : 22-triene, m. p. and mixed m. p. 172—175°, $[\alpha]_D$ +35°.

Preparation and Dehydration of 3β-*Acetoxyergosta*-7 : 22-*dien*-11β-*ol*.—Solutions of 3β-acetoxyergosta-7 : 22-dien-11-one (320 mg.) in ether–dioxan (5 : 1) (6 c.c.) and lithium aluminium hydride (0·45M) (2·5 c.c.) were mixed and then heated under reflux for 1 hr. The steroid was isolated in the usual way, and then acetylated at 20° overnight. Crystallisation from methanol–nitromethane (1 : 1) afforded 3β-*acetoxyergosta*-7 : 22-*dien*-11β-*ol* (210 mg.), m. p. 168—172°, $[\alpha]_D$ −21° (Found : C, 78·8; H, 10·3. $C_{30}H_{48}O_2$ requires C, 78·85; H, 10·6%). Dehydration of this compound (100 mg.) with phosphorus oxychloride (0·5 c.c.) in pyridine (3 c.c.) at 20°

gave a high yield of 3β-acetoxyergosta-7 : 9 : 22-triene, m. p. and mixed m. p. 172—175°, $[\alpha]_D$ +34°.

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Partial Reduction of Steroid Hormones and Related Substances.

By J. K. NORYMBERSKI and GILBERT F. WOODS.

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20-Ketones of the pregnane series and 17-ketones of the androstane series were preferentially reduced with sodium borohydride in the presence of the 4-en-3-one grouping. Reduction was stereospecific, giving the 20β- and 17β-hydroxy-epimers. Reduction of the 4-en-3-one grouping, when observed, gave rise to the 4-en-3β-ols, though in one instance reduction of the 4 : 5-olefinic bond occurred also.

PREFERENTIAL reduction of pregn-4-ene-3 : 20-diones at $C_{(20)}$, though known in biological systems (Caspi, Levy, and Hechter, *Arch. Biochem. Biophys.*, 1953, **45**, 169; Hayano, Wiener, and Lindberg, *Fed. Proc.*, 1953, **12**, 216; Hayano, Lindberg, Wiener, Rosenkrantz, and Dorfman, *Endocrinology*, 1954, **55**, 326), has not been hitherto accomplished by conventional chemical means. The partial reduction at $C_{(20)}$ has been brought about indirectly by protecting the 4-en-3-one grouping (cf. Romo, Romero, Djerassi, and Rosenkranz, *J. Amer. Chem. Soc.*, 1951, **73**, 1528; Sarett, Feurer, and Folkers, *ibid.*, p. 1777; Julian, Meyer, Karpel, and Cole, *ibid.*, p. 1982; Wendler, Huang-Minlon, and Tischler, *ibid.*, p. 3818; Antonucci, Bernstein, Heller, Lenhard, Littel, and Williams, *J. Org. Chem.*, 1953, **18**, 70) or by reducing both carbonyl groups and then oxidising the 4-en-3-ol grouping (Sondheimer, Amandolla, and Rosenkranz, *J. Amer. Chem. Soc.*, 1953, **75**, 5930).

The present work (cf. *Chem. and Ind.*, 1954, 518) concerns the action of sodium borohydride on compounds of the general type (I) and (IV). In exploratory experiments the extent to which cortisone acetate (I*a*) was reduced at $C_{(3)}$ and at $C_{(20)}$ severally was determined analytically. The results (see Table) show preferential reduction at $C_{(20)}$. On this basis a standard preparative method was developed wherein the reduction is performed with *ca.* 1·5 mol. of sodium borohydride in methanol at 0°.

Reduction of cortisone acetate in methanol.

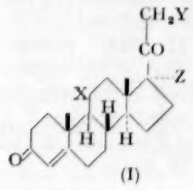
Concn. (mg./c.c.)	Temp.	$NaBH_4$ (mol.)	Reaction (%) at 3-one * 20 min.	at 3-one * 40 min.	at 20-one † 20 min.	at 20-one † 40 min.
2·5	0°	0·4	7	9	51	56
1·7	20	0·7	5	5	56	65
1·2	20	1·4	8	8	78	86
2·5	0	2·1	44	61	100	100
2·5	20	2·1	47	74	100	100

* Based on extinction at 238 mμ. † Measured as chromogen with phenylhydrazine–sulphuric acid (Porter and Silber, *J. Biol. Chem.*, 1950, **185**, 201).

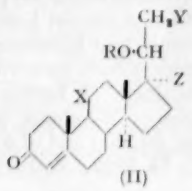
Reduction of cortisone acetate (I*a*) by the standard method and acetylation of the product gave 20β : 21-diacetoxy-17α-hydroxypregn-4-ene-3 : 11-dione (II*a*) (Reichstein's Substance U diacetate) (Reichstein and von Euw, *Helv. Chim. Acta*, 1941, **24**, 247E). Similarly, cortisol acetate (I*b*) gave 20β : 21-diacetoxy-11β : 17α-dihydroxypregn-4-en-3-one (IIb) (Reichstein's Substance E diacetate) (*idem, loc. cit.*).

Reduction of 11-deoxycorticosterone (I*c*), followed by acetylation, gave 20β : 21-diacetoxypregn-4-en-3-one (II*d*), $[M]_D$ +511°, which was hydrolysed to the diol (II*c*), $[M]_D$ +326°; and the latter was converted into its acetonyl derivative. The last two compounds, and their 20-epimers, have been previously prepared by different routes (Steiger and Reichstein, *ibid.*, 1938, **21**, 171; Julian, Meyer, and Printy, *J. Amer. Chem. Soc.*, 1948, **70**, 887) but their configuration at $C_{(20)}$ was not elucidated. This has now been done, as indicated, on the basis of the molecular rotation increment for (II*c* ⟶ II*d*) (cf. Sarett, *ibid.*, 1949, **71**, 1175; Klyne and Barton, *ibid.*, p. 1500). 3β : 20β : 21-Triacetoxypregn-4-ene (III*a*), $[M]_D$ +184°, was isolated as a by-product from the reduction of deoxycorticosterone (I*c*). The compound is considered to have been formed by way of the ketone (II*c*), hence the assignment of 20β-configuration. The configuration at $C_{(3)}$ is indicated by the negative shift of molecular rotation for (II*d* ⟶ III*a*) (cf. Mills, *J.*, 1952, 4976).

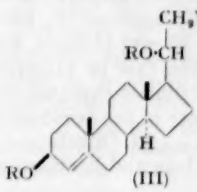
Reduction of progesterone (I*d*) afforded a mixture of 20β-hydroxypregn-4-en-3-one (II*e*), $[M]_D$ +280° {acetate (II*f*), $[M]_D$ +502°} (Wieland and Miescher, *Helv. Chim. Acta*, 1949, **32**, 1923), and pregn-4-ene-3β : 20β-diol (III*b*), $[M]_D$ +137°. The latter compound was further characterised by oxidation to the hydroxy-ketone (II*e*) by manganese dioxide (cf. Sondheimer *et al.*, *loc. cit.*). Reduction of 11-oxoprogesterone (I*e*) gave 20β-hydroxypregn-4-ene-3 : 11-dione (II*g*), $[M]_D$ +664° {acetate (II*h*), $[M]_D$ +811°}.



(I)



(II)



(III)

	X	Y	Z
(Ia) :	O	OAc	OH
(I*b*) :	OH	OAc	OH
(I*c*) :	H	OH	H
(I*d*) :	H	H	H
(I*e*) :	O	H	H

	X	Y	Z	R
(II*a*) :	O	OAc	OH	Ac
(II*b*) :	OH	OAc	OH	Ac
(II*c*) :	H	OH	H	H
(II*d*) :	H	OAc	H	Ac
(II*e*) :	H	H	H	H
(II*f*) :	H	H	H	Ac
(II*g*) :	O	H	H	H
(II*h*) :	O	H	H	Ac

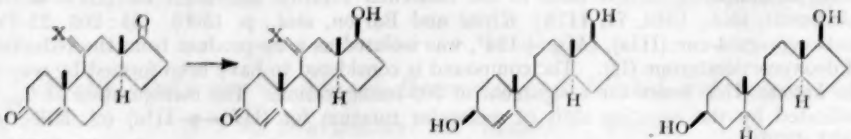
	Y	R
(III*a*) :	OAc	Ac
(III*b*) :	H	H

The results of the foregoing experiments suggested the possibility of partially reducing androst-4-ene-3 : 17-dione (IV*a*) to testosterone (V*a*) with sodium borohydride; owing to its importance, this conversion has received considerable attention: direct conversion has been accomplished by reduction with yeast (Mamoli and Vercellone, *Ber.*, 1937, **70**, 470) and by the Meerwein–Ponndorf method (Miescher and Fischer, *Helv. Chim. Acta*, 1939, **22**, 158) whilst all other preparative routes are indirect (for references see, *inter al.*, Fieser and Fieser, "Natural Products Related to Phenanthrene," 3rd Edn., Reinhold Publ. Corp., 1949, p. 371; Murray and Pederson, *J. Amer. Chem. Soc.*, 1952, **74**, 1239; Sondheimer *et al.*, *loc. cit.*; Dauben, jun., Loken, and Ringold, *ibid.*, 1954, **76**, 1359).

Reduction of the dione (IV*a*) with sodium borohydride, under the same conditions as in the pregnane series, gave testosterone (V*a*) in 60—70% yield. Androst-4-ene-3β : 17β-diol (VI), $[\alpha]_D$ +48° (Butenandt and Heusner, *Ber.*, 1938, **71**, 198), was obtained as a by-product. A further, apparently homogeneous, by-product (m. p. 152—154°, $[\alpha]_D$ +30°) gave with manganese dioxide a mixture of testosterone (V*a*) and androstane-3β : 17β-diol (VII), $[\alpha]_D$ +8°) and so is considered to be a molecular complex of (VI) and (VII). Its alternative composition from androst-4-ene-3α : 17β-diol and (VII) is ruled out on the basis of the former compound's high specific rotation ($[\alpha]_D$ +187°; Butenandt and Heusner, *loc. cit.*). [Reduction of the olefinic bond of androsten-4-ene-3 : 17-dione (IV*a*) by sodium borohydride has been already observed by Sondheimer, Velasco, Batres, and Rosenkranz (*Chem. and Ind.*, 1954, 1482).] The partial reduction of the dione (IV*a*) was also carried

out with potassium borohydride and with sodium trimethoxyborohydride: in both cases testosterone (V*a*) was obtained in good yield. Finally, 11-oxotestosterone (V*b*) (Herzog, Jevnik, Perlman, Nobile, and Hershberg, *J. Amer. Chem. Soc.*, 1953, **75**, 266) was obtained by the partial reduction of androst-4-ene-3 : 11 : 17-trione (IV*b*) with sodium borohydride.

The reactivities of steroid ketones towards sodium borohydride decrease in the order 3-one > 17- and 20-one > 4-en-3-one > 11-one (cf. Elisberg, Vanderhaeghe, and Gallagher,



(IV*a*): X = H_2
(IV*b*): X = O

(V*a*): X = H_2
(V*b*): X = O

(VI)

(VII)

ibid., 1952, **74**, 2814; Oliveto and Hershberg, *ibid.*, 1953, **75**, 488; Mancera, Ringold, Djerassi, Rosenkranz, and Sondheimer, *ibid.*, p. 1286; Soloway, Deutsch, and Gallagher, *ibid.*, p. 2356; Garrett and Lyttle, *ibid.*, p. 6051; this paper). It is worth noting that the sequence of the first four members of the above series is parallelled by that of their simple analogues arranged in order of decreasing oxidation potentials; *cyclo*hexanone (E_0 162 mv), *cyclo*pentanone (E_0 123 mv), *cyclo*hexyl methyl ketone (E_0 116 mv), and *cyclo*hex-2-enone (E_0 85 mv) (Adkins, Elofson, Rossow, and Robinson, *ibid.*, 1949, **71**, 3622); further, only in the case of 11-ketones are steric effects powerful enough to change the sequence of reactivities expected from this analogy. A further point of interest is the stereospecific course of the borohydride reduction of 20-ketones, irrespective of substitution at $C_{(17)}$ and at $C_{(21)}$ (cf. Oliveto and Hershberg, *loc. cit.*) and of 4 : 5-unsaturated 3-ketones (cf. Dauben, Micheli, and Eastham, *ibid.*, 1952, **74**, 3852; Zorbach, *ibid.*, 1953, **75**, 6344).

Experimental

Specimens for analyses were dried in a high vacuum for 16—24 hr. at 80—100°. M. p.s were determined on a Kofler stage. Unless otherwise specified rotations were measured in $CHCl_3$ (at 15—20°), ultraviolet absorption spectra in EtOH. For chromatography Peter Spence's Grade H alumina was neutralised as previously described (Brooks and Norymberski, *Biochem. J.*, 1953, **55**, 371).

Reductions with Sodium Borohydride. General Procedure.—A solution (0·4—0·6%) of the steroid in methanol (Burroughs' "A.R. quality") was treated with sodium borohydride (1·4—1·6 mol) for 1 hr. at 0°. Unless otherwise stated the mixture was worked up as follows. A few drops of acetic acid were added and the solution brought to dryness *in vacuo*. The residue was extracted with several portions of hot benzene or ethyl acetate. The crude product in benzene was absorbed on a column of alumina (100 parts) and subjected to gradient elution with benzene (50 c.c.)/benzene–ethyl acetate (1 : 1; 150 c.c.); 7-c.c. fractions were collected; finally the column was eluted with ethyl acetate (50—100 c.c.). In the following detailed descriptions the isolated products are recorded, under (i), (ii), &c., in the order of their elution from alumina.

Reduction of Cortisone Acetate (I*a*).—The acetate (200 mg.) was reduced by the general procedure. The mixture was concentrated *in vacuo* to a small volume, diluted with water, acidified with hydrochloric acid, and extracted with chloroform. The dry extract was acetylated with acetic anhydride in pyridine at 18°. The product was crystallised from acetone whereby 20β : 21-diacetoxy-17α-hydroxypregn-4-ene-3 : 11-dione (II*a*) (60 mg.) was obtained, having m. p. 248—251° (undepressed on admixture with material kindly provided by Prof. T. Reichstein), $[\alpha]_D$ +205° (*c*, 1·45), +179° (*c*, 0·86 in $COMe_2$), $\lambda_{max.}$ 237·5 mμ (ε 15,600), $\nu_{max.}$ 1741 [>C(OH)·CH(OAc)·CH_2·OAc], 1701 (11-C=O), 1665 (3-C=O), 1616 cm.$^{-1}$ (Δ^4) (in $CHCl_3$) (Found: C, 67·1; H, 7·6. Calc. for $C_{25}H_{34}O_7$: C, 67·2; H, 7·7%). Chromatography of the mother-liquors over alumina furnished a further 60 mg. of identical material.

Reduction of Cortisol Acetate (I*b*).—The reduction of this ester (200 mg.) was as above. Acetone (5 c.c.) was added, and the mixture concentrated *in vacuo* to a small volume, diluted

with water, and extracted with chloroform. Acetylation followed by chromatography over alumina and crystallisation from acetone furnished 20β : 21-diacetoxy-11β : 17α-dihydroxypregn-4-en-3-one (II*b*) (100 mg.) of m. p. 223—225° undepressed on admixture with material kindly provided by Prof. T. Reichstein. An analytical sample had m. p. 225—226°, $[\alpha]_D$ +169° (*c*, 0·65 in $COMe_2$), $\lambda_{max.}$ 239·5 mμ (ε 16,000), $\nu_{max.}$ 1740 [>C(OH)·CH(OAc)·CH_2·OAc], 1664 (3-C=O), 1619 cm.$^{-1}$ (Δ^4) (in $CHCl_3$) (Found : C, 67·3; H, 8·15. Calc. for $C_{25}H_{36}O_7$: C, 66·9; H, 8·1%).

Reduction of 11-*Deoxycorticosterone* (I*c*).—Reduction of this ketone (150 mg.) by the general procedure, followed by acetylation and chromatography gave : (i) 3β : 20β : 21-*Triacetoxypregn-4-ene* (III*a*) (50 mg.; m. p. 125—130°). Crystallisation from acetone–hexane afforded prisms, m. p. 128—131°, $[\alpha]_D$ +40° (*c*, 0·87), no selective absorption between 210 and 280 mμ, $\nu_{max.}$ 1731 (OAc) and 865 cm.$^{-1}$ (Δ^4) (in Nujol) (Found : C, 70·5; H, 8·7. $C_{27}H_{40}O_8$ requires C, 70·4; H, 8·75%). (ii) 20β : 21-*Diacetoxypregn-4-en-3-one* (II*d*) (100 mg.; m. p. 130—152°), blunt needles (from acetone–hexane), m. p. 155—156° (with melting and resolidification at 143—144°), $[\alpha]_D$ +123° (*c*, 0·95), +120° (*c*, 0·97 in $COMe_2$), $\lambda_{max.}$ 240·5 mμ (ε 17,400), $\nu_{max.}$ 1742, 1728 (OAc), 1669 (3-C=O), 865 cm.$^{-1}$ (Δ^4) (in Nujol) (Found : C, 72·25; H, 8·8. $C_{25}H_{36}O_5$ requires C, 72·1; H, 8·7%).

20β : 21-*Dihydroxypregn-4-en-3-one* (II*c*).—The diacetate (II*d*) (210 mg.) in methanol (25 c.c.) was treated with a solution of potassium hydroxide (1·2 g.) in aqueous methanol (25 c.c.; 90%) at 25° for 24 hr. under nitrogen. N-Hydrochloric acid (40 c.c.) was added; overnight crystals (37 mg.; m. p. 157—162°) separated which on recrystallisation from ether gave 20β : 21-dihydroxypregn-4-en-3-one (II*c*), m. p. 163—167°, $[\alpha]_D$ +98° [*c*, 0·86 in $CHCl_3$–EtOH (4 : 1)] (Found : C, 77·1; H, 9·6. Calc. for $C_{21}H_{32}O_3$: C, 75·9; H, 9·7%). Steiger and Reichstein (*loc. cit.*) recorded m. p. 166—167°, $[\alpha]_D$ +92·6° (in EtOH), for one of the epimeric 20 : 21-dihydroxypregn-4-en-3-one; Julian *et al.* (*loc. cit.*) found m. p. 166—168°, $[\alpha]_D$ +98° (in $CHCl_3$). Material (120 mg.) isolated from the aqueous mother-liquors by extraction with ethyl acetate was treated with zinc chloride in acetone (10 c.c.; 5% w/v) overnight at 20°. The crude product was chromatographed as described in the general procedure, except that the system benzene/benzene–ethyl acetate (4 : 1), was used for elution. The main fraction (50 mg.) afforded, on crystallisation from hexane, the *iso*propylidene derivative of the diol (II*c*) as prisms, m. p. 121—123°, $[\alpha]_D$ +94° (*c*, 1·09 in $COMe_2$), $\lambda_{max.}$ 240·5 mμ (ε 18,200) (Found : C, 77·25; H, 10·0. Calc. for $C_{24}H_{36}O_3$: C, 77·35; H, 9·75%). Steiger and Reichstein (*loc. cit.*) recorded m. p. 126°, $[\alpha]_D$ +91·5° (in $COMe_2$).

Reduction of Progesterone (I*d*).—Progesterone (350 mg.) was reduced by the general procedure; the following compounds were isolated. (i) Progesterone (215 mg.; m. p. 126—129°). A sample crystallised from ethanol had m. p. and mixed m. p. 127—129°, $[\alpha]_D$ +199° (*c*, 0·85 in EtOH). (ii) 20β-Hydroxypregn-4-en-3-one (II*e*) (110 mg., m. p. 153—172°), crystallised from acetone–hexane, had m. p. 173—175°, $[\alpha]_D$ +88° (*c*, 0·71), $\lambda_{max.}$ 240·5 mμ (ε 16,000), $\nu_{max.}$ 3480 (OH), 1670 (C=O), 1610, 860 cm.$^{-1}$ (Δ^4) (in Nujol) (Found : C, 79·5; H, 10·15. Calc. for $C_{21}H_{32}O_2$: C, 79·7; H, 10·2%), which with acetic anhydride in pyridine gave, after crystallisation from acetone–hexane, the acetate (II*f*) as leaflets, m. p. 164—165°, $[\alpha]_D$ +140° (*c*, 1·27), $\lambda_{max.}$ 241 mμ (ε 18,400) (Found : C 77·5; H, 9·65. Calc. for $C_{23}H_{34}O_3$: C, 77·05; H, 9·55%). The recorded physical constants of (II*e* and *f*) agree with those reported by Wieland and Miescher (*loc. cit.*), Turner and Voitle (*J. Amer. Chem. Soc.*, 1951, **73**, 2283), and Sondheimer, Amandolla, and Rosenkranz, *ibid.*, 1953, **75**, 5930).

In a second experiment a further, less readily eluted product was isolated. It crystallised from acetone–hexane in prisms, m. p. 178—180°, $[\alpha]_D$ +43° (*c*, 1·3). In spite of an unsatisfactory analysis (Found : C, 77·8; H, 10·9. Calc. for $C_{21}H_{34}O_2$: C, 79·2; H, 10·8%) the compound is formulated as pregn-4-ene-3β : 20β-diol (III*b*). Its treatment with manganese dioxide in chloroform (cf. Sondheimer *et al.*, *loc. cit.*) furnished 20β-hydroxypregn-4-en-3-one (II*e*) identified by m. p., mixed m. p., and $[\alpha]_D$ +94° (*c*, 1·08).

Reduction of 11-*Oxoprogesterone* (I*e*).—Reduction of the dione (250 mg.) by the general procedure gave : (i) 11-Oxoprogesterone (I*e*) (15 mg.) identified by m. p., mixed m. p., and $[\alpha]_D$ +250° (*c*, 0·60). (ii) 20β-*Hydroxypregn-4-ene-3* : 11-*dione* (II*g*) (96 mg.; m. p. 167—187°). Crystallisation from acetone–hexane gave prisms, m. p. 197—200°, $[\alpha]_D$ +201° (*c*, 0·94), $\lambda_{max.}$ 236 mμ (ε 17,300) (Found : C, 76·0; H, 9·1. $C_{21}H_{30}O_3$ requires C, 76·3; H, 9·15%), which gave an *acetate* (II*h*), plates (from acetone–hexane), m. p. 205—207°, $[\alpha]_D$ +218° (*c*, 0·81), $\lambda_{max.}$ 236 mμ (ε 17,800) (Found : C, 74·1; H, 8·55. $C_{23}H_{32}O_4$ requires C, 74·15; H, 8·65%).

Reduction of Androst-4-ene-3 : 17-*dione* (IV*a*).—By the general procedure this dione gave : (i) Testosterone (V*a*) (170 mg.; m. p. 147—154°). A sample crystallised from acetone–hexane

had m. p. and mixed m. p. 154—155°, $[\alpha]_D$ +110° (*c*, 0·7 in EtOH), $\lambda_{max.}$ 240·5 mμ (ε 16,800) (Found : C, 79·3; H, 10·0. Calc. for $C_{19}H_{28}O_2$: C, 79·1; H, 9·8%); the infrared spectrum was identical with that of authentic material. (ii) and (iii) A mixture of diols (35 mg.) which was combined with similar material from replicated preparations : the aggregate (116 mg.) was separated on alumina into two main fractions. The fraction (50 mg.) more readily eluted crystallised from acetone–ethyl acetate in needles, m. p. 162—163°, $[\alpha]_D$ +48° [*c*, 1·14 in $CHCl_3$–EtOH (1 : 1)], no selective absorption above 210 mμ (Found : C, 78·8; H, 10·5. Calc. for $C_{19}H_{30}O_2$: C, 78·55; H, 10·4%), considered to be androst-4-ene-3β : 17β-diol (VI). Butenandt and Heusner (*loc. cit.*) recorded m. p. 153—154°, $[\alpha]_D$ +48·5° (in EtOH). Treatment with manganese dioxide in chloroform (cf. Sondheimer *et al.*, *loc. cit.*) afforded testosterone (V*a*) 90% by spectroscopic evidence), identified by m. p., mixed m. p., $[\alpha]_D$ +108° (*c*, 0·93), $\lambda_{max.}$ 240 mμ (ε 16,500). The fraction (56 mg.) less readily eluted from alumina crystallised from acetone–hexane in prisms, m. p. 152—154°, $[\alpha]_D$ +30·5° [*c*, 0·83 in $CHCl_3$–EtOH (1 : 1)], no selective absorption above 210 mμ [Found : C, 75·95; H, 11·0. $C_{19}H_{30}O_2$,$C_{19}H_{32}O_2$,H_2O (?) requires C, 75·95; H, 10·7%]. Treatment of this material with manganese dioxide in chloroform gave testosterone (V*a*) (50% by spectroscopic evidence). Chromatography over alumina gave, in order of elution, (*a*) testosterone, m. p. and mixed m. p. 152—154°, $[\alpha]_D$ +108° (*c*, 0·88 in EtOH), $\lambda_{max.}$ 240·5 mμ (ε 16,100), and (*b*) androstane-3β : 17β-diol (VII), m. p. 166—167° undepressed on admixture with authentic material (kindly provided by Dr. W. Klyne from the M.R.C. Steroid Reference Collection), $[\alpha]_D$ +8° (*c*, 0·36 in EtOH); the infrared spectrum was identical with that of authentic material. (iv) Sparingly soluble material (10 mg.) which from methanol afforded fine needles, m. p. 217—233°, $[\alpha]_D$ +70° (*c*, 0·3 in dioxan). Further characterisation of this material was not attempted. Repeated reductions of the dione (IV*a*) with sodium borohydride regularly furnished 60—70% of pure testosterone, 15—25% of the diol fraction, and 5—10% of the sparingly soluble material.

Reduction of the dione (IV*a*) (200 mg.) with potassium borohydride (27 mg., 0·7 mol.) at 22° under otherwise unchanged conditions afforded testosterone (135 mg.), identified by m. p., mixed m. p., and $[\alpha]_D$ +110° (*c*, 0·95 in EtOH).

Reduction of the dione (IV*a*) (200 mg.) with sodium trimethoxyborohydride (360 mg., 4·0 mol.) under otherwise unchanged conditions gave : (i) Androst-4-ene-3 : 17-dione (45 mg.), identified by m. p., mixed m. p., and $[\alpha]_D$ +191° (*c*, 0·61 in EtOH). (ii) Testosterone (130 mg.), identified by m. p., mixed m. p., and $[\alpha]_D$ +109° (*c*, 0·75 in EtOH).

Reduction of Androst-4-ene-3 : 11 : 17-*trione* (IV*b*).—Reduction of this trione (100 mg.) by the general procedure gave 11-oxotestosterone (V*b*) (45 mg.; m. p. 182—186°). Crystallisation from acetone–hexane afforded needles, m. p. 186·5—188°, $[\alpha]_D$ +199° (*c*, 0·68 in $COMe_2$), $\lambda_{max.}$ 237·5 mμ (ε 16,500), $\nu_{max.}$ 3460—3420 (OH), 1703 (11-C=O), 1665 (3-C=O), 1618 cm.$^{-1}$ (Δ^4) (in $CHCl_3$) (Found : C, 75·4; H, 8·9. Calc. for $C_{19}H_{26}O_3$: C, 75·45; H, 8·65%). The recorded physical constants are in good agreement with those reported by Herzog *et al.* (*loc. cit.*), Herr and Heyl (*J. Amer. Chem. Soc.*, 1953, **75**, 5927), Bernstein, Lenhard, and Williams (*J. Org. Chem.*, 1953, **18**, 1166), and Mancera, Sondheimer, and Rosenkranz (*J.*, 1953, 2189).

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Exchange Reactions and Magnetic Susceptibilities of Complex Salts. Part II. Magnetic Susceptibilities of Some Complex Nickel Salts.*

By H. C. Clark and A. L. Odell.

[Reprint Order No. 51014.]

Magnetic susceptibilities over a temperature range of 100° have confirmed that bis-salicylaldoximenickel and bis-*N*-methylsalicylaldiminenickel form in pyridine solution complexes which presumably are octahedral and contain two pyridine molecules per nickel atom. Measurements of bis-salicylaldehyde-*o*-phenylenedi-iminenickel and bis-salicylaldiminenickel in pyridine solution show the occurrence of temperature-dependent equilibria between dia- and para-magnetic forms which appear to be respectively planar and octahedral. Equilibria also occurred in solutions of bis-*N*-methylsalicylaldiminenickel in chloroform, benzene, toluene, and *m*-xylene, where the two forms are more probably planar and tetrahedral respectively. Calculations have been made of the equilibrium constants; hence the heats of reaction, free energy, and entropy changes have been obtained and related to the structural changes involved in the equilibria.

The validity of the distinction made by magnetic measurements between covalent and ionic bonds in metallic complexes has been widely discussed in recent years. It is now generally accepted that covalent bonding, utilising the hybrid-bond systems suggested by Pauling (*J. Amer. Chem. Soc.*, 1931, **53**, 1391), results in increased electron pairing and hence a reduction in the magnetic moment.

The nature of the co-ordinate link in highly paramagnetic salts is less certain and has been variously described as " ionic " and " covalent involving outer *d* orbitals " (Huggins, *J. Chem. Phys.*, 1937, **5**, 527) while Taube (*Chem. Rev.*, 1952, **50**, 69) and others have suggested the use of $4s4p^34d^2$ hybrid orbitals. Craig, Maccoll, Nyholm, Orgel, and Sutton (*J.*, 1954, 332) have made overlap integral calculations for this type of bonding and have shown that such bonds are highly polar, and not very different in character from " ionic " bonds. Resonance is then possible between covalent and ionic forms, so that the magnetic moment gives no indication of the covalent contribution to the bonding. Magnetic-susceptibility determinations thus divide complexes into (*a*) a class using inner *d* orbitals which give rise to essentially covalent bonds and (*b*) a class in which the bonds are highly polar.

Values of the magnetic moment intermediate between the values for the two alternative modes of spin coupling are very rare and hence interest was centred on the values reported by Willis and Mellor (*J. Amer. Chem. Soc.*, 1947, **69**, 1237) for complexes of nickel and derivatives of salicylaldehyde in various solvents. The majority of these complexes were diamagnetic as solids, but solvents such as pyridine, chloroform, benzene, and dioxan caused changes to paramagnetism with values of approximately 2 B.M., these values being independent of concentration. However, the magnetic susceptibilities had been observed at only one temperature. A further investigation of these susceptibilities has therefore been made over a wide temperature range.

Discussion of Results.—Attempts to extend the ranges of solvents and concentrations were restricted by the low solubilities; however, certain new results were added to those of Willis and Mellor. All these determinations were made at 298° K.

The results in Table 1 thus confirm the occurrence of these intermediate values of the magnetic moments as well as their concentration independence.

Temperature dependence. Eight solutions were investigated over a temperature range, the results being given in Tables 2 and 3.

For the pyridine solutions of bis-salicylaldoximenickel and bis-*N*-methylsalicylaldiminenickel, the plots of $1/\chi_M$(corr.) against T are straight lines giving values of 30° and 40° respectively for the molecular field constants. For the remaining compounds, all were

* Part I, *J.*, 1954, 63.

TABLE 1.

Compound	Solvent	Concn. × 10^5	χ_M(corr.) × 10^6	B.M.	Solvent	Concn. × 10^5	χ_M(corr.) × 10^6	B.M.
Bis-salicylaldoxime-nickel	C_5H_5N	1558	4004	3·10	$CHCl_3$	313	1203	1·70
	"	869	3890	3·05				
Bis-salicylaldiminenickel	C_5H_5N	718	1921	2·15	C_5H_5N	511	1984	2·18
Bis-*N*-methylsalicylald-iminenickel	C_5H_5N	4690	3934	3·07	Dioxan	1891	1944	2·16
		2365	3999	3·10		1465	1825	2·09
		1145	4061	3·12		1180	1822	2·09
	$CHCl_3$	2158	1587	1·95		676	1693	2·02
		1025	1532	1·92	C_6H_6	1852	1359	1·81
		520	1596	1·96	C_6H_5Me	783	810	1·40
	EtOH	206	2729	2·56	*m*-$C_6H_4Me_2$	855	300	0·85
Bis-salicylaldehyde-ethyl-enedi-iminenickel	C_5H_5N	841	0	Diamag.				
Bis-salicylaldehyde-*o*-phenylenedi-iminenickel	C_5H_5N	795	2293	2·35	$CHCl_3$	193	0	Diamag.
		629	2308	2·35				

TABLE 2. *Corrected molar susceptibilities (c.g.s. units* × 10^6). *Solvent: pyridine.*

Temperature (°K)	198°	257°	273°	298°	316°
Bis-salicylaldoximenickel	5686	4370	4204	3953	3714
Bis-*N*-methylsalicylaldiminenickel	5552	4266	4111	3922	3720
Bis-salicylaldiminenickel	5473	3708	3151	1954	1151
Bis-salicylaldehyde-*o*-phenylenedi-iminenickel	6289	3327	2911	2312	1477

TABLE 3. *Corrected molar susceptibilities of bis-*N*-methylsalicylaldiminenickel in various solvents.*

Solvent	198°	250°	273°	298°	323° K
Chloroform	5767	3922	3037	1546	860
Benzene	—	—	3050	1358	503
Toluene	5615	4173	1900	811	—
m-Xylene	—	2839	1176	300	—

fully paramagnetic with moments of 2·95—3·20 B.M. at 198° K, but above this temperature the Curie–Weiss law was not obeyed and apparent equilibria were observed between dia- and para-magnetic forms, the former predominating at the higher temperatures.

Willis and Mellor suggested that in pyridine solutions, the change to paramagnetism is due to the formation of octahedral complexes as follows:

$$[Ni(C_7H_6O_2N)_2] + 2py \rightleftharpoons [Ni(C_7H_6O_2N)_2py_2] \qquad (py = pyridine)$$

They were unable to isolate the pyridine addition derivatives of any of the above compounds, but Basolo and Matoush (*J. Amer. Chem. Soc.*, 1953, **75**, 5663) have since obtained certain of these derivatives by slow crystallisation from pyridine solutions. We were able to isolate pyridine adducts of bis-salicylaldoximenickel and bis-*N*-methylsalicylaldiminenickel by the addition of excess of water to the pyridine solutions. The precipitates so obtained could be dried without decomposition over calcium chloride and the loss of weight on heating at 110° C for several hours was then determined. For the adduct of bis-salicylaldoximenickel, the fraction of weight lost was 0·348 (Calc. for loss of two molecules of pyridine from $[Ni(C_7H_6O_2N)_2py_2]$: 0·325). Similarly for the adduct of bis-*N*-methylsalicylaldiminenickel, the observed fraction of weight lost was 0·327, compared with a calculated loss of 0·328.

Hence, in the pyridine solutions of the above two compounds there is complete formation of paramagnetic pyridine adducts which contain two pyridine molecules per nickel atom and presumably utilise the highly polar outer sp^3d^2 octahedral configuration.

For the remaining pyridine solutions, the magnetic measurements show the occurrence of temperature-dependent equilibria between dia- and para-magnetic forms. These equilibria also probably occur between diamagnetic planar forms and octahedral pyridine adducts, the latter being less stable at higher temperatures, so that their formation is incomplete. The lower stability of the pyridine adducts of bis-salicylaldiminenickel and bis-salicylaldehyde-*o*-phenylenedi-iminenickel is not unexpected since Basolo and Matoush

were unable to isolate them. In view of the strong co-ordinating power of pyridine it is unlikely that the equilibrium would be between planar and tetrahedral forms.

The remaining solutions contain bis-*N*-methylsalicylaldiminenickel dissolved in typical non-polar solvents such as benzene, chloroform, toluene, and *m*-xylene, where normal co-ordination of solvent molecules is improbable.

Nyholm recently suggested (*Chem. Rev.*, 1953, **53**, 263) that for some complexes the planar arrangement of the solid may be partly due to the effect of intermolecular forces, which may be reduced in solution, allowing the isolated molecule to assume the shape of lowest potential energy. For nickel complexes this would apparently be the tetrahedral configuration. The energy difference between the planar and tetrahedral structures may therefore be small, allowing the natural occurrence of a thermal equilibrium.

That the equilibrium in these non-co-ordinating solvents is between planar and tetrahedral forms has already been suggested by Willis and Mellor and later by Basolo and Matoush. The latter workers observed intermediate values of the magnetic moment of bisformylcamphorethylenedi-iminenickel in methylbenzene solvents and it is probable that here also a temperature-dependent equilibrium occurs. They conclude that the effect is not due to solvation since no correlation can be drawn between the base strength of the solvent and the amount of paramagnetism.

The results obtained for bis-*N*-methylsalicylaldiminenickel in methylbenzene solvents show considerable similarity to those for bisformylcamphorethylenediaminenickel, although the susceptibilitiy at 25° shows a more marked decrease with change of solvent. Again no correlation can be drawn between the base strength, as given by McCaulay and Lien (*J. Amer. Chem. Soc.*, 1951, **73**, 2013), and the amount of paramagnetism; indeed, it seems probable that the decrease in paramagnetism as the solvent is changed from benzene to toluene to *m*-xylene is rather an effect of the increasing asymmetry of the solvent molecules. Although not conclusively proved, it thus seems probable that in these solvents the equilibrium is between planar and tetrahedral forms.

Susceptibility determinations over a temperature range for ethyl alcohol and dioxan solutions of bis-*N*-methylsalicylaldiminenickel were not made owing to the low solubility and hence the large errors in alcohol, and to the high freezing point (11° c) of dioxan. However, in these solvents, co-ordination of the solvent molecules is possible, so the paramagnetic form may be either octahedral or tetrahedral.

Where applicable, it is obviously possible to define the equilibrium constant as $K = [\text{Diamagnetic}]/[\text{Paramagnetic}]$. From purely paramagnetic susceptibilities at 198° K, the susceptibilities of the pure paramagnetic form at 316°, 298°, 273°, and 250° K could be calculated, the molecular field constants being assumed to be zero. Values of K thus obtained are given in Table 4.

TABLE 4.

Compound	Solvent	257°	273°	298°	316°
(1) Bis-salicylaldiminenickel	Pyridine	0·17	0·27	0·87	1·97
(2) Bis-salicylaldehyde-*o*-phenylenedi-iminenickel	Pyridine	0·46	0·57	0·81	1·67
(3) Bis-*N*-methylsalicylaldiminenickel	Chloroform	0·25	0·38	1·48	2·69
		250°	273°	298°	323°
(4) Bis-*N*-methylsalicylaldiminenickel	Benzene	—	0·35	1·79	5·94
(5) " " " "	Toluene	0·08	1·18	3·35	—
(6) " " " "	*m*-Xylene	0·59	2·51	11·6	—

The plots of $\log_{10} K$ against $1/T$ were straight lines within experimental error, and hence approximate values for the heats of reaction were calculated. The free-energy change could also be calculated from the relation $\Delta G = RT \log_e K$. The entropy changes were obtained by using the equation $\Delta G = \Delta H - T\Delta S$.

Solution	ΔH (cal.)	ΔG (at 25°)	ΔS (e.u.)	Solution	ΔH (cal.)	ΔG (at 25°)	ΔS (e.u.)
(1)	7960	30	27	(4)	9990	− 380	35
(2)	3740	−125	13	(5)	10,700	− 980	39
(3)	7210	−360	25	(6)	9060	−1500	35

The errors in these values are higher than for results obtained by other methods, the values for ΔS having an error of approximately ± 15—20%. For solutions (2) and (5) the

error may be slightly larger, and it is therefore possible to obtain only an indication of the meaning of the entropy changes.

For solutions (1) and (2) solvation appears to be involved and the equilibrium can be represented as

$$[Ni(C_7H_6ON)_2py] \rightleftharpoons [Ni(C_7H_6ON)_2] + 2py$$

The entropy increase is probably due to the large increase in the number of free particles. The results may be compared with the work of Calvin and Bailes (*J. Amer. Chem. Soc.*, 1946, **68**, 958) who obtained for the reaction

$$[Ni(NH_3)_6]^{2+} + 3en\ (aq.) \rightleftharpoons [Ni(en)_3]^{2+} + 6NH_3\ (aq.)$$

where there is an increase of three in the number of particles, the value $\Delta S = 24$ e.u.

For the remaining solutions, the equilibrium is more probably between planar and tetrahedral forms. The fact that the conversion from the paramagnetic into the diamagnetic configuration is an endothermic reaction supports Nyholm's suggestion that for certain complexes in solution the tetrahedral form is the state of lowest energy. Nor is the entropy change inconsistent with this suggestion. It is probable that the electric dipole moment of the tetrahedral form is responsible for the association of a number of solvent molecules. On conversion into the planar *trans*-form, this dipole disappears, with the liberation of excess of associated solvent molecules, accompanied by an increase in entropy (cf. Chatt and Wilkins, *J.*, 1952, 273). However, it is doubtful whether this effect would be great enough fully to account for the comparatively large entropy change.

Experimental

Preparation and Analysis of Compounds.—The compounds investigated were prepared by the general methods of Pfeiffer (*Annalen*, 1933, **503**, 84). Each compound was analysed for nickel and nitrogen content, the nitrogen being determined by the standard Kjeldahl method and the nickel by precipitation with dimethylglyoxime.

Ni complex with	Formula	Found (%) N	Found (%) Ni	Calc. (%) N	Calc. (%) Ni
Salicylaldoxime	$Ni(C_7H_6O_2N)_2$	8·49	17·63	8·47	17·75
Salicylaldimine	$Ni(C_7H_6ON)_2$	9·47	19·61	9·37	19·65
N-Methylsalicylaldimine	$Ni(C_8H_8ON)_2$	8·43	17·72	8·56	17·95
Salicylaldehyde-ethylenedi-imine	$Ni(C_{18}H_{14}O_2N_2)$	8·52	17·93	8·63	18·05
Salicylaldehyde-*o*-phenylenedi-imine	$Ni(C_{20}H_{14}O_2N_2)$	7·41	15·68	7·52	15·75

The solvents used in the magnetic measurements were of " AnalaR " grade or were carefully dried and purified by standard methods.

Magnetic Measurements.—Magnetic susceptibilities were determined with the use of a Gouy-type magnetic balance, the current through the electromagnet being regulated within 0·002%.

Susceptibilities were determined at 316°, 298°, 273°, 257° (or 250°), and 198° K. The two highest temperatures were maintained by the use of a water thermostat, and at 273° by ice–water. A solid carbon dioxide–acetone freezing mixture was used at 198° K. For measurements at 257°, use was made of ice–salt freezing mixtures, and at 250° melting carbon tetrachloride was used, although both these cases probably involved a slightly larger error in temperature.

The apparatus was calibrated with acetone, benzene, and freshly-boiled, distilled water, French and Trew's susceptibility values (*Trans. Faraday Soc.*, 1945, **41**, 439) being used.

The susceptibilities of the complexes were determined from the differences between those of the pure solvents and the solutions, according to the formula

$$\chi_{g(complex)} = [\chi_{g(solvent)}(1-x) - \chi_{g(solution)}]/x$$

where x = fraction by weight of complex in solution. After calculation of the molar susceptibilities, corrections for the diamagnetism of the ligands were made by using Pascal's constants (Selwood, " Magnetochemistry," Interscience Publishers Inc., New York, 1943, pp. 51—55).

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Exchange Reactions and Magnetic Susceptibilities of Complex Salts. Part III. Exchange Reactions of Some Nickel Complex Salts.*

By H. C. Clark and A. L. Odell.

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The synthesis and use in exchange studies of [*carbonyl*-^{14}C]salicylaldehyde is described. In pyridine solutions, rapid and complete exchange of the active ligands of bis-salicylaldoximenickel and bis-*N*-methylsalicylaldiminenickel and bis-salicylaldiminenickel was observed, while zero exchange occurred with bis-salicylaldehyde-ethylenedi-iminenickel and bis-salicylaldehyde-*o*-phenylenedi-iminenickel. The results are correlated with the magnetic susceptibilities.

The mechanisms of isotopic exchange reactions of complex compounds have recently been discussed by Taube (*Chem. Rev.*, 1952, **50**, 69), Adamson and Wilkins (*J. Amer. Chem. Soc.*, 1954, **76**, 3379), and MacDiarmid and Hall (*ibid.*, p. 4222). For the "outer orbital" type of octahedral complex, where highly polar sp^3d^2 hybrid bonds occur, the exchange mechanism probably involves the dissociation of a ligand grouping, the energy required for such a dissociation being offset by the removal of a relatively unstable 4*d* orbital from hybridisation. Slow exchange will generally be expected for "inner orbital" complexes except where an available low-energy orbital allows the formation of an activated intermediate complex of low energy and higher co-ordination number. Exceptional cases may occur where stereochemical requirements outweigh the effect of electronic structure and bond type and cause large activation energies. Thus fairly slow rates of ligand exchange will generally be expected for quadridentate ligands (Ruben, Kamen, Allen, and Nahinsky, *ibid.*, 1942, **64**, 2297).

Part II (*loc. cit.*) gave the results of magnetic measurements on solutions of several nickel complexes. The present paper contains the results of ligand-exchange studies with these same solutions. Exchange of the central nickel atom of these complexes has been investigated by Johnson and Hall (*ibid.*, 1948, **70**, 2344) and Hall and Willeford (*ibid.*, 1951, **73**, 5419), using radioactive nickel, and it was hoped that this investigation of ligand exchange would remove several anomalous results.

Complex	Time (min.)	Relative activity of complex	Relative activity of ligand	Ratio of rel. act.
Bis-salicylaldoximenickel	5	1192	1095	1·09
	10	1142	1128	1·01
	15	1176	1128	1·04
Bis-salicylaldiminenickel	5	985	935	1·05
	10	960	935	1·02
	60	975	935	1·04
Bis-*N*-methylsalicylaldiminenickel	5	1152	1125	1·02
	10	1170	1125	1·04
	60	1170	1125	1·04
Bis-*N*-methylsalicylaldiminenickel *	1	956	950	1·00
	5	958	908	1·05
	60	960	950	1·00
" " " †	5	955	905	1·05
	10	998	965	1·03
Bis-salicylaldehyde-ethylenedi-iminenickel	10	98	2484	0·03
	60	164	2440	0·07
	1440	130	2530	0·02
Bis-salicylaldehyde-*o*-phenylenedi-iminenickel	10	161	2180	0·07
	60	224	2080	0·10
	300	225	2020	0·11
	5400	112	2210	0·05

* In dioxan. † In ethyl alcohol.

Discussion of Results.—Activity determinations were made on infinitely thick samples with the apparatus and procedure described in Part I (*J.*, 1954, **63**). The results in the Table

* Part II, preceding paper.

show the relative activities of complex and free ligands expressed as counts per equiv. of salicylaldehyde per minute. The solvent was pyridine except in the two cases noted.

Discussion.—In pyridine solution bis-salicylaldoximenickel forms a paramagnetic octahedral pyridine adduct (see Part II), presumably using $4s4p^34d^2$ hybrid orbitals. The observed rapid exchange would thus be expected and probably occurs as follows:

(*a*) $[Ni(ligand)_2py_2] \rightleftharpoons [Ni(ligand)_2] + 2py$ (py = pyridine)

(*b*) $[Ni(ligand)_2] + (ligand)^* \rightleftharpoons [Ni(ligand)_2(ligand)^*]$

(*c*) $[Ni(ligand)_2(ligand)^*] \rightleftharpoons [Ni(ligand)(ligand)^*] + (ligand)$

(*d*) $[Ni(ligand)(ligand)^*] + 2py \rightleftharpoons [Ni(ligand)(ligand)^*py_2]$

This stepwise mechanism is postulated since reactions (*a*) and (*c*), involving a decrease in the co-ordination number from six to four, would temporarily remove the two high-energy 4*d* orbitals from hybridisation. Hence the activation energy would be small, leading to rapid exchange.

However, this mechanism would require the two pyridine molecules to occupy *cis*-positions to allow the entry of the third ligand. Hence the ligand molecules must be rearranged as the complex enters solution or during the exchange process since the solid complex has a planar structure. Such a rearrangement is possible since Dwyer and Mellor (*J. Amer. Chem. Soc.*, 1941, **63**, 81) showed that the dipyridine derivative of bisdiazoaminobenzenenickel has two pyridine molecules occupying *cis*-positions. Bis-*N*-methylsalicylaldiminenickel in pyridine solution also formed an octahedral dipyridine compound. In agreement with observation, rapid exchange proceeding by the above mechanism would also be expected here.

In ethyl alcohol, dioxan, chloroform, and methylbenzene solutions, temperature-dependent equilibria occurred. In chloroform and methylbenzene solutions the paramagnetic form is probably tetrahedral, while in ethyl alcohol and dioxan, either an octahedral or a tetrahedral form is consistent with the observed exchange rates. Unfortunately, no exchange studies could be made in chloroform or methylbenzene solutions, owing to the lack of a suitable separation procedure.

As a solid, bis-salicylaldehyde-ethylenedi-iminenickel is diamagnetic and hence planar. In pyridine solution it is diamagnetic and may be planar or may form a dipyridine-octahedral complex with a $3d^24s4p^3$ hybrid bond system involving the promotion and pairing of two electrons in the 5*s* orbital as suggested by Burstall and Nyholm (*J.*, 1952, 3570). Both of these structures would result in the observed diamagnetism and a negigible substitution rate. (For this and the following complex, the observed complex activities were probably due to contamination caused by incomplete separation.)

The observed zero exchange of bis-salicylaldehyde-*o*-phenylenedi-iminenickel in pyridine solution was unexpected in view of the magnetic measurements, although Hall and Willeford had also observed a slow rate of substitution of the central nickel atom. Attempts to formulate an exchange mechanism explain to some extent this inertness. As the ligand is quadridentate and planar, the paramagnetic form observed in pyridine solution is unlikely to have a tetrahedral structure but instead is probably octahedral with two pyridine molecules occupying *trans*- rather than *cis*-positions. Two substitution mechanisms can be suggested, the first involving the dissociation of the complex by the simultaneous breaking of all four bonds between the nickel atom and the ligand, *i.e.*, a simple collision mechanism. This would require considerable energy and the activation energy would probably be so high as to prohibit substitution of either ligand or metal.

The second possible mechanism would involve the formation of an activated intermediate complex with the nickel atom increasing its co-ordination number from six to eight so as to hold two ligand molecules simultaneously. Since there are no suitable low-energy orbitals for such an increase, and since it would be extremely difficult to arrange two such planar ligands around one nickel atom, the activation energy would again be high, causing very slow substitution rates. Stereochemical requirements also prohibit the formation of an activated intermediate containing two ligand groupings, each bound by, say, two bonds to the nickel atom.

In contrast to the zero exchange of the nickel complex, West (*J.*, 1954, 395) has ascribed the slow exchange of the corresponding cobalt complex and the very rapid exchange of the zinc complex (Atkins and Garner, *J. Amer. Chem. Soc.*, 1952, **74**, 3527) to differences in solvation, but the different electronic structures of these metals and hence the widely differing stabilities of the planar, tetrahedral, and octahedral configurations will also influence the exchange rates.

So the observed rates of ligand substitution can all be correlated with the magnetic susceptibilities and hence with the electronic structure of the central nickel atom, except where the large activation energy, arising from stereochemical considerations, outweighs the influence of the electronic structure.

Experimental

Preparation of [carbonyl-^{14}C]*Salicylaldehyde.*—This synthesis was carried out in three stages: (*a*) carboxylation of *o*-methoxyphenylmagnesium bromide to *o*-anisic acid by use of $^{14}CO_2$; (*b*) reduction of *o*-anisoyl chloride to *o*-methoxybenzaldehyde; and (*c*) demethylation of the aldehyde to [*carbonyl*-^{14}C]salicylaldehyde.

(*a*) A solution of *o*-methoxyphenylmagnesium bromide in ether–benzene (1 : 1) was prepared under nitrogen from *o*-bromoanisole (4 g.) and magnesium (0·58 g.). The concentration of the resulting solution was found by titration to be 0·268M, corresponding to a 91% yield of the Grignard reagent.

The carboxylation of 25-ml. samples of this solution was carried out in a vacuum-apparatus similar to that described by Dauben, Reid, and Yankwich (*Analyt. Chem.*, 1947, **19**, 828), the carbon dioxide being generated from active barium carbonate (25 μc). For efficient stirring during carboxylation, a modification of the stirrer described by Joseph (*Ind. Eng. Chem. Anal.*, 1937, **9**, 212) was used. Carboxylation was complete within 20—30 min. The mixture was then hydrolysed with dilute hydrochloric acid and ice, and the ethereal layer extracted six times with 5% sodium hydrogen carbonate solution. On acidification white crystals of *o*-anisic acid were obtained in 60% yield based on barium carbonate.

(*b*) The acid chloride was then prepared by refluxing the *o*-anisic acid with purified thionyl chloride for 5 hr., the excess of thionyl chloride being removed under reduced pressure. The acid chloride was reduced to the aldehyde by means of the apparatus and procedure described by Reid and Jones (*J. Biol. Chem.*, 1948, **174**, 427), the reaction being followed by the evolution of hydrogen chloride, which was passed through standard alkali. The yield of aldehyde obtained in the active preparation was 71% of the theoretical.

(*c*) The active *o*-methoxybenzaldehyde was demethylated by Prey's method (*Ber.*, 1942, **75**, 445): it was refluxed at 200° for 45 min. with dry pyridine hydrochloride (1·3 g.), and the hot solution then poured with rapid stirring into 2N-hydrochloric acid (40 ml.). The resultant solution was extracted with ether, and the ethereal layer extracted with aqueous potassium hydroxide solution. The final active product was obtained in ethereal solution by acidification of the alkaline extract and extraction with ether. The yield of salicylaldehyde in pilot runs was 30—45% as estimated by formation of the 2 : 4-dinitrophenylhydrazone. Thus the overall yield was approximately 18% based on barium carbonate. All other methods of demethylation resulted only in resin.

The solution for use in exchange experiments was obtained by the addition of 3 g. of pure non-active salicylaldehyde to the final ethereal extract.

Preparation of the Active Ligands.—The active Schiff's bases of salicylaldehyde with ethylenediamine and *o*-phenylenediamine were prepared in 95% yield from concentrated alcoholic solutions of the aldehyde and the corresponding diamine. The other Schiff's bases were not isolated, but were prepared in solution in the required solvent by the addition of the estimated quantities of the various amines to the aldehyde solution.

Separation Procedures.—Four slightly different procedures were employed.

(*a*) From the pyridine solution of bis-salicylaldoximenickel and active salicylaldoxime, the complex was precipitated by addition of excess of water, filtered off, and washed with alcohol. The free salicylaldoxime was then precipitated with nickel acetate solution.

(*b*) Bis-salicylaldiminenickel and bis-*N*-methylsalicylaldiminenickel were separated from their respective free ligands by dilution with sodium chloride solution. The filtrate was acidified, and the free ligands were precipitated as the 2 : 4-dinitrophenylhydrazone, which was filtered off and washed.

(*c*) Salicylaldehyde-ethylenedi-imine was separated from the nickel complex by addition of a limited amount of water. After the free Schiff's base had been filtered off, excess of water was added to the filtrate, precipitating the complex, which was washed with alcohol to remove any remaining traces of free ligand.

(*d*) Bis-salicylaldehyde-*o*-phenylenedi-iminenickel was precipitated from the pyridine solution (15 ml.) on the addition of a small volume of water (7·5 ml.). This precipitation was incomplete but sufficient to provide infinitely thick counting samples. On the addition of excess of water to the filtrate, a mixture of the free ligand and complex was precipitated, this being filtered off and discarded. The final filtrate was acidified, and the 2 : 4-dinitrophenylhydrazone of the free ligand precipitated.

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Partial Molar Quantities at Infinite Dilution in Dissociating Solvents.

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Gibbs's discussion of chemical potentials at infinite dilution is applied directly to dissociating solvents, for which the result $(\partial\mu_1/\partial m_2)_0 = 0$, discussed by Dunning and Dunning (*J.*, 1952, 2993), follows immediately (m_2 refers to a dissociation product). An alternative demonstration of this theorem, making direct reference to dissociation equilibria, and yet avoiding the limitations of Dunning and Dunning's methods, is also described. The formula $(\partial\bar{X}_1/\partial m_2)_0 = 0$ applies generally to the other common partial molar quantities, and the curvature of the rate of change of any of these quantities at the composition of the pure solvent is given by the expression $m_1(\partial^2\bar{X}_1/\partial m_2^2)_0 = -(\partial\bar{X}_2/\partial m_2)_0$.

IN a paper on the thermodynamics of dissociating solvents (*J.*, 1952, 2993), Dunning and Dunning discuss the effects of complex forms of dissociation upon the proof that $(\partial\mu_1/\partial m_2)_{T,\,P,\,m_1} = 0$ when $m_2 = 0$ (the suffixes 1 and 2 referring respectively to the solvent and to a solute which is a product of the dissociation of the solvent). This part of their paper invites comment for two reasons. First, it may give the misleading impression that specific reference to involved equations referring to complex equilibria is necessary to establish the general validity of the result that $(\partial\mu_1/\partial m_2) = 0$ when $m_2 = 0$. Secondly, one of their methods of obtaining this result (*loc. cit.*, p. 2995) seems to be open to criticism, since to make the assertion at any stage of the proof that $(\partial\mu_2/\partial m_2)$ is not infinite when $m_2 = 0$ is, by the Gibbs–Duhem equation (1) equivalent to asserting that

$$m_1(\partial\mu_1/\partial m_2) + m_2(\partial\mu_2/\partial m_2) = 0 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$(\partial\mu_1/\partial m_2)_0 = 0$ which is what is to be proved. It would seem therefore that either such an assertion should be avoided or, if it is regarded as self-evident, a direct appeal should be made to (1) to establish that $(\partial\mu_1/\partial m_2)_0 = 0$ before proceeding to the useful discussion of the second derivative to examine the extent of the curvature of the function of μ_1 with m_2.

Gibbs's Method.—Such a simple result as that required seems, however, to demand a much more direct proof, and it is curious that Gibbs's relevant discussion should have been ignored by later writers. Gibbs ("Collected Works," Vol. I, Longmans Green, New York, 1928, p. 111) first establishes that for stability with regard to continuous changes μ_i must be an increasing function of m_i, and then shows that $(\partial\mu_1/\partial m_2)$ must be zero when $m_2 = 0$ "if m_2 is capable of negative as well as positive values" (*op. cit.*, p. 135). This argument is quite general and independent of any chemical reactions in the solution; and the example

discussed by Gibbs, namely the addition of water to a salt hydrate (*op. cit.*, p. 136), could equally well have involved the hydrate of dinitrogen pentoxide Once this argument is accepted, the more complicated discussions by later writers seem only to verify the internal consistency of the equations used to characterize the chemical equilibria involved.

An Alternative Demonstration making Direct Mention of Chemical Equilibria.—The alternative argument which follows is free from the restriction of Dunning and Dunning's first method (*loc. cit.* p. 2994) since it is not limited to slightly dissociated solvents.

Let S be a dissociating solvent for which the dissociation equilibrium can be represented by the chemical equation

$$iA + jB + kC \ldots\ldots\ldots \rightleftharpoons S \quad \ldots\ldots\ldots \quad (2)$$

where i, j, k refer to the numbers of molecules of A, B, C, . . . formed by the dissociation of one molecule of S : they may be simple fractions when necessary (*e.g.*, $\frac{1}{2}H_2O + \frac{1}{2}N_2O_5 \rightleftharpoons HNO_3$). The products A, B, C, . . . may themselves dissociate further to any extent (even completely) since the argument is only concerned with the partial molar free energy of the substance A, etc., as it exists in the solction. The condition of chemical equilibrium gives :

$$i\mathrm{d}\mu_A + j\mathrm{d}\mu_B + k\mathrm{d}\mu_C \ldots\ldots = \mathrm{d}\mu_S \quad \ldots\ldots\ldots \quad (3)$$

Variations in the quantity of the dissociation product A only being considered :

$$i(\partial\mu_A/\partial m_A) + j(\partial\mu_B/\partial m_A) + k(\partial\mu_C/\partial m_A) \ldots = (\partial\mu_S/\partial m_A) \quad \ldots \quad (4)$$

We note that the equations (3) and (4) will in fact hold even if the solvent is completely dissociated since the removal of 1 mole of S from the solution would involve the same operation as the removal of i moles A + j moles B + etc.

The solution may also be regarded in terms of the dissociation products as thermodynamic components; the Gibbs–Duhem equation will then apply in the following form :

$$m_A(\partial\mu_A/\partial m_A) + m_B(\partial\mu_B/\partial m_A) + m_C(\partial\mu_C/\partial m_A) + \ldots = 0 \quad \ldots \quad (5)$$

Now as the composition of the pure solvent is approached, the ratio $m_A : m_B : m_C \ldots$. will approach the ratio $i : j : k \ldots$ and at the exact composition of S, the left-hand sides of equations (4) and (5) will become identical (apart from an unimportant arbitrary multiplier) whatever the values of the individual differential coefficients. Hence it follows that the right-hand side of (4), namely $(\partial\mu_S/\partial m_A)$, must be identical with the right-hand side of (5), *i.e.* zero. The same obviously applies also to $(\partial\mu_S/\partial m_B)$, etc. This demonstration will hold for a dissociating solvent which is a compound of any number of components and is dissociated to any extent.

Ionic species of dissociation products present no special difficulty in either of the above methods when the electroneutrality condition is obeyed (Guggenheim, " Modern Thermodynamics," Methuen, London, 1933, p. 133; or " Thermodynamics, 2nd Ed., North-Holland Publishing Co., Amsterdam, 1950, pp. 296, 330). Thus on the addition of potassium nitrate to nitric acid, for example, the nitrate ion, being capable of positive and negative increments (subject to the condition of electroneutrality), will have no effect initially on the chemical potential of the solvent; whilst the potassium ion, being capable of only positive increments, will produce an initial effect similar to that of a foreign non-electrolyte.

Curvature of the Solvent Potential–Composition Function at Infinite Dilution.—It is possible to express the curvature of function of the solvent chemical potential and other partial molar quantities with composition in a simple, yet exact, form in the neighbourhood of the pure solvent composition.

Further differentiation of equations (4) and (5) with respect to m_A, and elimination of the terms $(\partial^2\mu_i/\partial m_i^2)$ after multiplication of the derivative of (4) by $\alpha = m_A/i = m_B/j$, etc., yields, when $m_A : m_B : m_C \ldots = i : j : k \ldots$:

$$\alpha(\partial^2\mu_S/\partial m_A^2) = -(\partial\mu_A/\partial m_A) \quad \ldots\ldots\ldots \quad (6)$$

By changing the notation and regarding the solvent as component 1 and the solute (a dissociation product of 1) as component 2, we may differentiate equation (1) and obtain :

$$m_1(\partial^2\mu_1/\partial m_2^2) = -(\partial\mu_2/\partial m_2) - m_2(\partial^2\mu_2/\partial m_2^2) \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

Equation (7), unlike equation (6) which refers only to the composition of the pure solvent, is quite general and exact. Comparison with equation (6), however, shows that, when $m_2 = 0$, $(\partial^2\mu_2/\partial m_2^2)$ cannot be infinite (which could clearly have been deduced in other ways); so that at $m_2 = 0$ (represented by suffix 0) :

$$m_1(\partial^2\mu_1/\partial m_2^2)_0 = -(\partial\mu_2/\partial m_2)_0 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

Since μ_2 is an increasing function of m_2, $\partial\mu_2/\partial m_2$ is positive and (8) therefore formally shows μ_1 to be at a maximum. (The identification of equations (6) and (8) rests, of course, on the fact that differential coefficients with respect to changes in the mass of a given substance are independent of the choice of the other components in the system, as explained by Gibbs, *op. cit.*, p. 92—93.) Dunning and Dunning's equation (28) is an approximate, special form of equation (8); and a similar argument to theirs relating the curvature expressed by equation (8) to the degree of dissociation obviously follows. For if the potential depends roughly logarithmically upon the actual quantity of A present, there will obviously be a larger increment in μ_2 per mole of A added when there is a small amount of A in the pure solvent (slightly dissociated) than when there is a large amount (highly dissociated).

Other Partial Molar Quantities.—The condition that $(\partial\mu_1/\partial m_2)_0 = 0$ is clearly independent of the temperature and pressure provided that these remain constant during the differentiation. Therefore

$$\partial/\partial T(\partial\mu_1/\partial m_2)_0 = \partial/\partial m_2(\partial\mu_1/\partial T)_0 = -(\partial\bar{S}_1/\partial m_2)_0 = 0 \quad . \quad . \quad . \quad (9)$$

and

$$\partial/\partial P(\partial\mu_1/\partial m_2)_0 = -(\partial\bar{V}_1/\partial m_2)_0 = 0 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (10)$$

Also, since $\mu_1 = \bar{H}_1 - T\bar{S}_1$:

$$(\partial\bar{H}_1/\partial m_2)_0 = 0 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (11)$$

Differentiation of (11) with respect to temperature also gives

$$(\partial\bar{C}p_1/\partial m_2)_0 = 0 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (12)$$

Thus, all the common partial molar quantities of a dissociating solvent in mixtures involving only dissociation products are of Lewis and Randall's " first type " (" Thermodynamics, etc.," McGraw Hill, 1923, p. 44).

By similar methods the second differential coefficients can all be shown to follow the same pattern as for the solvent potential (8), *i.e.* :

$$m_1(\partial^2\bar{X}_1/\partial m_2^2)_0 = -(\partial\bar{X}_2/\partial m_2)_0 \quad . \quad . \quad . \quad . \quad . \quad . \quad (13)$$

where X represents any partial molar quantity. Whether equation (13) represents a maximum or a minimum in $\bar{X}_1$ depends upon the characteristics of the dissociation process. If the solutions can be regarded as ideal when the dissociation has been allowed for, $\bar{H}_1$ will be given approximately by $\bar{H}_1' + x\Delta H_d$, where $\bar{H}_1'$ is the solvent partial molar heat content when the dissociation is completely suppressed, x the fractional extent of dissociation, and ΔH_d the heat of dissociation. (The cryoscopic implications of this formulation have been discussed in an earlier paper; Wyatt, *J.*, 1953, 1175.) Thus whether equation (13) represents a maximum or a minimum in $\bar{H}_1$ depends upon whether the dissociation is endothermic or not; and corresponding arguments apply to the other partial molar quantities, which can be formulated similarly, *e.g.* $\bar{V}_1 = \bar{V}_1' + x\Delta V_d$. The possibility of a point of inflection in $\bar{H}_1$, etc., does not seem to be absolutely excluded, since it is possible to imagine an addition compound's having a heat of dissociation of zero at the composition

of the pure compound, and yet having dissociation products which cause thermal non-ideality of opposite signs on opposite sides of this composition. In general, however, $\bar{H}_1$ would be expected to exhibit a maximum or a minimum, and $\bar{H}_2$ would then have the characteristic S-shaped curve found by Kunzler and Giauque for water in sulphuric acid (*J. Amer. Chem. Soc.*, 1952, **74**, 3472), since it follows from the analogue of equation (I), and the value of $(\partial\bar{H}_2/\partial m_2)_0$, that when m_2 is positive $\bar{H}_1$ and $\bar{H}_2$ will vary in opposite directions, whilst when m_2 is negative $\bar{H}_1$ and $\bar{H}_2$ will vary in the same direction. [The author's former discussion of partial molar heat contents in sulphuric acid (*loc. cit.*, p. 1178) was in error on this point, and the cryoscopic behaviour of non-electrolytes in this solvent therefore seems to demand a less simple explanation than that involving a variable cryoscopic constant; cf. Wyatt, *J.*, 1954, 2647.]

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Geometrical Isomerism of the Azonaphthalenes.

By MAX FRANKEL, REUVEN WOLOVSKY, and ERNST FISCHER.

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cis-2 : 2′- and *cis*-1 : 2′-Azonaphthalene have been prepared by irradiation of the solutions of the corresponding *trans*-isomers with ultraviolet light, isolated by chromatography on alumina at low temperature, and characterized by their absorption spectra; *cis*-1 : 1′-azonaphthalene has been similarly prepared and characterized in solution containing up to 60% of *cis*-isomer : it was not isolated. The dipole moments of *cis*-2 : 2′- and of *trans*-2 : 2′- and *trans*-1 : 1′-azonaphthalene were determined.

THE formation of *cis*-azobenzene during irradiation of solutions of the *trans*-isomer was first reported by Hartley (*Nature*, 1937, **140**, 281). Later (Hartley, *J.*, 1938, **633**; Cook, *J.*, 1938, 876; Cook, Jones, and Polya, *J.*, 1939, 1315; Hartley and Le Fèvre, *J.*, 1939, 531), the isolation and the properties of this isomer were described in detail. (For a survey see Campbell, Henderson, and Taylor, *J.*, 1953, 1281.) Attempts to isolate the *cis*-isomers of the azonaphthalenes seem, however, to have failed hitherto (Cook and Jones, *J.*, 1939, 1311; Brode, Gould, and Wyman, *J. Amer. Chem. Soc.*, 1952, **74**, 4645).

The present paper describes the preparation and characteristic properties of *cis*-1 : 1′-, *cis*-2 : 2′-, and *cis*-1 : 2′-azonaphthalene, the isolation of the last two by adsorption on alumina at low temperature, and the separation of *cis*- and *trans*-2 : 2′-azonaphthalene by chromatography on paper.

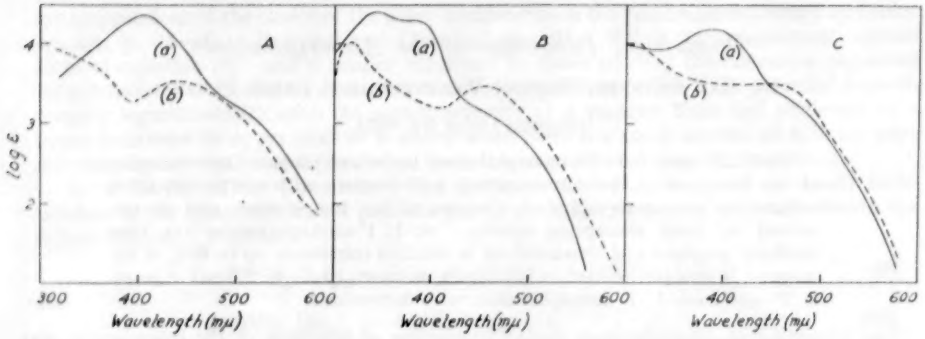
Preliminary spectrophotometric experiments showed that at room temperature the effect of ultraviolet irradiation on solutions of the three ordinary azonaphthalenes is extremely short-lived, and that a rapid thermal reversion to the original form takes place. When irradiation and spectrophotometric measurements were carried out at −25°, pronounced changes of the visible and near ultraviolet absorption spectrum were observed which were reversed at rates depending on the temperature, the solutions finally exhibiting absorption spectra identical with those observed before irradiation. The reversions proved to be first-order reactions, with the half-life times $\tau_{1/2}$, and the critical increments E_A in toluene given in the Table.

Azonaphthalene	Temp.	$\tau_{1/2}$ (min.)	Temp.	$\tau_{1/2}$ (min.)	E_A, kcal. mole^{-1}
1 : 1′-	0°	173	12·5°	29·5	22 ± 2
2 : 2′- •	29·0	150	47·0	19	22 ± 2
1 : 2′-	18·5	104	45·0	5	21 ± 2

• In chloroform at 41° $\tau_{1/2}$ = 12 min.

These figures may be compared with Hartley's results (*J.*, 1938, 638) for the thermal *cis* ⟶ *trans*-conversion of azobenzene in benzene, as follows : $\tau_{1/2}$ at 56·5° = 150 min. and at 76·6° = 21 min., E_A = 23 kcal. mole.

On the strength of the above results, all the operations in the experiments undertaken to isolate the *cis*-isomers of 2 : 2′- and of 1 : 2′- azonaphthalenes were carried out at 0° in a dimly lit room. Toluene or chloroform solutions of the two compounds were irradiated and then passed through a column packed with activated alumina. Subsequent development with the same solvent produced in each of these cases two separate zones. The lower zones were washed through the column, and the upper zones eluted with the solvent containing about 1% of methanol. Evaporation of the two solutions thus obtained from each of these azonaphthalenes and subsequent drying in a high vacuum produced two compounds in each case; with 2 : 2′-azonaphthalene the orange compound (*a*) derived from the lower zone had a m. p. of 209°. The reddish compound (*b*) derived from the upper zone, upon being heated in the normal procedure in a m. p. apparatus, changed colour from reddish to orange before melting and finally melted at 209°. If (*b*) was placed in the m. p. apparatus preheated to a temperature not far below the m. p. of (*a*), besides



[Absorption spectra in toluene:

A, 1 : 1′-Azonaphthalene at −25°
B, 2 : 2′-Azonaphthalene at + 8° } (*a*) = *trans*-, ————
C, 1 : 2′-Azonaphthalene at −25° } (*b*) = *cis*-, – – – –

	A		*B*		*C*	
	(*a*)	(*b*)	(*a*)	(*b*)	(*a*)	(*b*)
Max.	405 mμ (log ε 4·33)	440 mμ (log ε 3·5)	345 mμ (log ε 4·37)	315 mμ (log ε 4·0) 450 mμ (log ε 3·45)	385 mμ (log ε 4·2)	310 mμ (log ε 4·0)
Inflexion.....	*ca.* 500 mμ (log ε *ca.* 3·2)	*ca.* 350 mμ (log ε *ca.* 3·7)	*ca.* 385 mμ (log ε *ca.* 4·25) *ca.* 460 mμ (log ε *ca.* 3·1)		*ca.* 460 mμ (log ε *ca.* 3·3)	*ca.* 420 mμ (log ε *ca.* 3·5)

the change of colour, liquefaction followed by immediate solidification occurred, before the m. p. of 209° was reached. On resolidification, the substance showed no m. p. depression when mixed with a sample of (*a*).

A similar phenomenon was observed with 1 : 2′-azonaphthalene: The red compound (*a*) derived from the lower zone, when heated slowly, melted at 144—145°. The orange-red compound (*b*) derived from the upper zone, upon being heated in the m. p. apparatus, became red before melting at 144—145°. On introduction of (*b*) into the preheated m. p. apparatus, besides the change in colour, a momentary liquefaction and resolidification was observed and finally melting occurred at 144—145°. Again, no m. p. depression was observed with mixtures of resolidified samples of (*a*) and (*b*).

It appears that in both cases, on heating, a conversion of the *cis*-form (*b*) into the *trans*-form (*a*) takes place.

The Figure shows the absorption spectra of the *cis*- and *trans*-isomers of 1 : 1′-, 1 : 2′-, and 2 : 2′-azonaphthalene. In general, the type of the curves for the *cis*- and

trans-forms agree with those found in other cases of *cis*- and *trans*-isomers of similar azo-compounds.

The dipole moments of the two isomers of 2 : 2′-azonaphthalene were zero for (*a*) in toluene at 30°, and 3·0 ± 0·1 D for (*b*) in toluene at 0°, in agreement with the *trans*- and *cis*-configuration assigned to them. Hartley and Le Fèvre (*J.*, 1939, 531) report for the *trans*- and *cis*-isomers of azobenzene in benzene zero and 3D, respectively.

The data for 1 : 1′-azonaphthalene in the Table indicate that isolation of the *cis*-isomer might be possible in this case only by working at temperatures considerably below 0°. The following procedure was adopted in order to calculate the approximate absorption spectrum of the *cis*-isomer.

The dielectric constant increment $(\delta\varepsilon)_a = \varepsilon_{\text{solution}} - \varepsilon_{\text{solvent}}$ of a toluene solution of the (assumed) *trans*-isomer leads to a molar polarisation at infinite dilution of the solute, $(_\infty P_2)_{trans}$, corresponding to zero moment. Irradiation (to completion) of the solution at −25° causes a further increment $(\delta\varepsilon)_b$. From the combined increments $(\delta\varepsilon)_a + (\delta\varepsilon)_b$ the polarisation at infinite dilution of the (assumed) mixture of *cis*- and *trans*-isomers, $_\infty P_2$, is derived. The fraction of *cis*-isomer will then be given by:

$$[_\infty P_2 - (_\infty P_2)_{trans}]/[(_\infty P_2)_{cis} - (_\infty P_2)_{trans}].$$

It being assumed that $(_\infty P_2)_{cis}$ equals the polarisation observed for the pure *cis*-isomer of 2 : 2′-azonaphthalene, insertion of experimental figures leads to a fraction of 0·60 ± 0·05 of *cis*-isomer in the above conditions. The absorption curve (*b*) of the pure *cis*-isomer (*A* in Fig.) was reconstructed from the curves found for the pure *trans*-isomer before and after irradiation at −25°, assuming that 60% of the *trans*- is converted into *cis*-isomer.

A paper-chromatographic technique analogous to that described for azobenzene (Frankel and Wolovsky, *Experientia*, 1954, **10**, 356) was used as an auxiliary method for the micro-separation and estimation of the two isomers of 2 : 2′-azonaphthalene.

Results of irradiation of azobenzene and the three azonaphthalenes at wavelengths other than 365 mμ will be reported separately.

Experimental

All work with solutions was carried out in a dimly lit room at 0°. M. p.s were determined in a Fisher–Johns apparatus.

Preparation of Azonaphthalenes.—1 : 1′-Azonaphthalene, prepared from 1-naphthylamine (Friedlaender, "Fortschritte der Theerfarbenfabrikation und verwandter Industriezweige," 1899, **4**, 1016; Nietzki and Goll, *Ber.*, 1885, **18**, 297, 3252) and recrystallised from xylene and from dioxan, had m. p. 190°. 2 : 2′-Azonaphthalene, prepared from 2-naphthylamine according to Friedlaender (*loc. cit.*) and recrystallised from toluene, had m. p. 209°. 1 : 2′-Azonaphthalene was prepared from 4-amino-1 : 2′-azonaphthalene (Nietzki and Goettig, *Ber.*, 1887, **20**, 612; Cook, Hewett, Kennaway, and Kennaway, *Amer. J. Cancer*, 1940, **40**, 62). On recrystallisation from glacial acetic acid followed by one from *n*-heptane, dark red needles were obtained (Found: C, 84·7; H, 5·0; N, 9·3. Calc. for $C_{20}H_{14}N_2$: C, 85·1; H, 5·0; N, 10·0%). We found m. p. 144—145° on slow heating, and 136° on placing the sample in the preheated m. p. apparatus. Nietzki and Goettig (*loc. cit.*) reported m. p. 136°; Cook, Hewett, *et al.* (*loc. cit.*) give 144—145°. This compound seems to exist in at least two crystalline forms.

The three azo-compounds used as starting materials throughout the present experiments were purified chromatographically at room temperature from their chloroform solutions in a column packed with activated alumina.

Adsorption Chromatography.—Columns were packed with "Fischer Scientific Co. Activated Alumina (for Absorbing), 8—14 M" ground in a mortar. Passage of the solutions through the column was accelerated by applying suction.

Irradiation.—Irradiations were carried out with a Mazda type MBW/U 125-w mercury-vapour discharge lamp, emitting 95·5% of its radiation at 365 mμ.

cis-2 : 2′-*Azonaphthalene.*—*trans*-2 : 2′-Azonaphthalene (0·2 g.) in chloroform (100 ml.) was irradiated in an evaporating dish from a distance of 5 cm. for about 3 hr. The solution, which had become red and contained about 70% of the *cis*-isomer, was passed through a column (40 cm. long, 3 cm. internal diam.) of activated alumina. All unchanged *trans*-isomer was washed through the column with 200 ml. of chloroform, while the *cis*-isomer remained adsorbed

in a sharp zone 10 cm. long, beginning at 5 cm. from the top of the column. The zone containing the adsorbed material was eluted in portions with a total of 250 ml. of chloroform containing about 1% of methanol, and the resulting solutions were filtered and evaporated in the cold. The irradiation and all the following manipulations were carried out in the dark at 0°, and attempts were made to attain the solid state as quickly as possible.

cis-1 : 2′-*Azonaphthalene.*—*cis*-1 : 2′-Azonaphthalene was prepared in the same way as *cis*-2 : 2′-azonaphthalene. The isolated *cis*-compounds were kept in the dark at low temperature.

Chromatography on Paper of 2 : 2′-*Azonaphthalene.*—The ascending method was applied, strips or sheets of Whatman No. 1 filter paper being used throughout. A drop of the solution containing both isomers was placed on the paper. When working at room temperature, glacial acetic acid, or, at low temperature, glacial acetic acid–ethanol (1 : 3, v/v), was used as the mobile phase. A yellow spot containing the *cis*-isomer rapidly migrates upwards, while a yellow spot containing the *trans*-isomer remains stationary.

Spectrophotometric Technique.—All measurements and most irradiations were carried out in the special Dewar-type cells described by Hirshberg and Fischer (*J.*, 1953, **629**; 1954, **297**, 3129). In each experiment, the concentration was checked by re-measuring the absorption spectrum after heating the solution, in the cell, for ½ hr. at about 90° and recooling to room temperature (at 90° rapid conversion into the *trans*-isomer occurs).

Dielectric-constant Increments, and Results of Dipole-moment Measurements.—The method used at 30° has been described by Bergmann, Weizmann, and Fischer (*J. Amer. Chem. Soc.*, 1950, **72**, 5009). For measurements involving irradiations of the solutions *in situ* a modified Sayce–Briscoe cell was used, the contents of which could be mixed by alternative application of suction and pressure to one of the side-arms, in an atmosphere of dry nitrogen. The cell was placed in a large unsilvered Dewar flask filled either with water and crushed ice (for work at 0°) or with ethanol (for work below 0°). The ethanol bath was cooled below the desired temperature by liquid nitrogen introduced at a controlled rate into a copper container immersed in the bath. Thermoregulation to ±0·02° was in this case achieved by means of a mercury-in-glass thermoregulator, controlling the current in a heating element placed at the bottom of the bath. In the following summary of the results, Le Fèvre's nomenclature and method of calculation (Harris, Le Fèvre, and Sullivan, *J.*, 1953, 1622) are used. Owing to the low solubility of both *trans*-azonaphthalenes, the increments of dielectric constant, $\delta\varepsilon$, density, δd, and index of refraction, δn_D, were measured only at one concentration, in toluene at 30°, with the following results :

	10^4w	$10^4\delta\varepsilon$	$10^4\delta n_D$	$10^4\delta d$
trans-1 : 1′-Azonaphthalene	105	60	—	25
trans-2 : 2′-Azonaphthalene	82	45	22	19·5

These figures yield the following empirical constants, molar polarisations, ${}_\infty P_2$, and molar refraction, ${}_\infty R_2$, at infinite dilution :

Azonaphthalene	$C\alpha\varepsilon_1$	β	$C'\gamma n_1^2$	${}_\infty P_2$ (ml.)	${}_\infty R_2{}^D$ (ml.)
trans-1 : 1′-	0·105	0·28	—	103·5 ± 3	—
trans-2 : 2′-	0·102	0·28	0·158	102·5 ± 3	113 ± 3

The molar refraction R^D calculated for azonaphthalene from bond refractivities (Vogel *et al.*, *J.*, 1952, 514) is about 93 ml. The observed ${}_\infty R_2$ is probably somewhat increased by anomalous dispersion (Bergmann, Fischer, and Jaffe, *J. Amer. Chem. Soc.*, 1953, **75**, 3230), whereas R^D may be too low because in its calculation the resonance between the two halves of the molecule is ignored. In view of the difficulty in assessing the effect of these factors, it may be concluded that the orientation polarisation, and therefore the dipole moment, is zero for both *trans*-compounds.

For *cis*-2 : 2′-azonaphthalene the following results were obtained in toluene at 0° :

10^4w	3·1	14·9	20·6	29·7	36·7	42·1
$10^4\delta\varepsilon$	37	69	93	135	162	187

whence $\delta\varepsilon = 4{\cdot}70w - 65w^2$, and $({}_\infty P_2)_{cis} = 307$ ml. If the observed $({}_\infty P_2)_{trans} = 102{\cdot}5$ ml. is taken as equal to the distortion polarisation, we get an apparent moment in toluene of 3·02 ± 0·05D.

For 1 : 1′-azonaphthalene in toluene at −25° and a weight fraction of $w = 0{\cdot}0029$, the observed $\delta\varepsilon$ before irradiation was 0·0034, increasing to 0·0107 after irradiation. The latter

value leads to an apparent molar polarisation ${}_{\infty}P_2$ of 244·5 ml. for the assumed mixture of *cis*- and *trans*-isomers.

Thanks are expressed to Dr. Y. Hirshberg in whose laboratory the spectrophotometric determinations were carried out.

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Stereospecificity in the Perkin–Oglialoro Reaction. The Stereochemical Configurations of Some Substituted α-Phenylcinnamic Acids.

By Malcolm Crawford and G. W. Moore.

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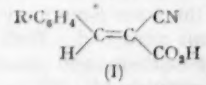
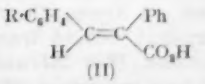
The Perkin–Oglialoro reaction is found to give with various aromatic aldehydes the corresponding α-phenylcinnamic acids, of *trans*-configuration (with respect to aryl and carboxyl groups as in cinnamic acid). Salicylaldehyde is an exception and nitro-aldehydes give rise to some *cis*-acid. Configurations allotted previously to these acids have been confirmed in some cases, and revised in others, and some new acids have been examined. Factors affecting the stereochemical course of the reaction are discussed.

Baker and Howes (*J.*, 1953, 119) showed that condensation of salicylaldehyde or its methyl ether with cyanoacetic acid or its ester gives only the isomers (I; R = *o*-Me or *o*-OH) with the *trans*-configuration (with respect to aryl and carboxyl groups). This agrees with what would be expected on steric grounds, for in these products the bulkiest groups are at a distance. It is surprising, therefore, to find that in the rather similar aldehyde condensation, namely Oglialoro's modification (*Gazzetta*, 1878, **8**, 429) of the Perkin reaction, the main and usually the only product has *cis*-arrangement of the bulkiest groups. Oglialoro's modification consists merely in using sodium phenylacetate in place of acetate in the Perkin reaction. The product of the condensation of various aryl aldehydes with phenylacetic anhydride under these conditions is the *trans*-acid (II; R = H, *o*-, *m*-, or *p*-NO_2, OH, or OMe) in all cases except from salicylaldehyde, though when R = H or NO_2 small amounts of the *cis*-isomers (III) are also formed. In the *trans*-


(I)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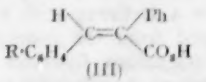
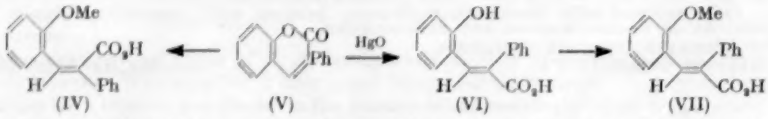

(III)

isomer (II) the bulkiest groups (Ph being assumed to be bulkier than CO_2H) are *cis* with respect to one another, which must involve a measure of steric compression greater than in the *cis*-isomer (III). Apparently therefore the relative stability of the possible products is not the determining factor in the stereochemical course of this reaction. Before pursuing this, however, it is essential to be sure of the configurations of the products. These have been established for the new acids and confirmed for those of doubtful structure as follows.

ortho-*Acids.*—*cis*-*o*-Methoxy-α-phenylcinnamic acid (IV), m. p. 131·5°, has been prepared for the first time by the methylation of 3-phenylcoumarin (V), and its configuration is thus established. The *trans*-acid (VII), m. p. 184°, was obtained from 3-phenylcoumarin by isomerisation with yellow mercuric oxide (see Sen and Chakravarti, *J. Indian Chem. Soc.*, 1929, **6**, 852), followed by methylation of the (new) *trans*-*o*-hydroxy-α-phenylcinnamic acid (VI) first formed. Compound (VII) does not depress the m. p. of a sample prepared by Funk and Kostanecki's method (*Ber.*, 1905, **38**, 939). They held it to be the *cis*-acid.

meta-*Acids.*—The configurations of *cis*- and *trans*-*m*-amino-α-phenylcinnamic acids

have now been definitely established by diazotisation and reduction to the corresponding deaminated acids (II and III; R = H) of known configuration (Stoermer and Prigge, *Annalen*, 1915, **409**, 13). The structures of the *m*-amino-acids determine those of the *m*-nitro-acids from which they were prepared and of the *m*-hydroxy-acids into which they were converted.



The *cis*-hydroxy-acid is new. The *trans*-acid has m. p. 187° which differs considerably from the various values in the literature. The *m*-methoxy-α-phenylcinnamic acids were prepared from the hydroxy-acids: the *cis*-acid is new and the configuration previously assigned to the *trans*-acid is found to be correct (Funk and Kostanecki, *loc. cit.*; Kon and Spickett, *J.*, 1949, **2724**).

para-*Acids.*—Condensation of *p*-nitrobenzaldehyde with phenylacetic acid gave *cis*- and *trans*-*p*-nitro-α-phenylcinnamic acids in the ratio of about 1 : 4 (see Bakunin, *Gazzetta*, 1895, **25**, 137), from which the two amino-acids (new) were obtained on reduction. Their configurations have been established similarly to those of the *m*-amino-acids. Surprisingly the *cis*-nitro-acid, m. p. 143°, on reduction gives about equal quantities of *cis*- and *trans*-amino-acid, thus indicating that some stereomutation occurs during reduction. By a diazo-reaction the *cis*-amino-acid gives a nitro-acid of m. p. 127°, which depresses the m. p. of the *trans*-nitro-acid but not that of the *cis*-isomer; this is assumed to be a modification of the *cis*-acid similar to those of *allo*cinnamic acid; on reduction it gives only the *trans*-amino-acid. The *cis*-*p*-amino-acid shows, therefore, a marked stereolability.

Of the *p*-hydroxy-α-phenylcinnamic acids only the *trans*-form had previously been prepared (Zincke and Geibel, *Annalen*, 1906, **349**, 110) by Perkin–Oglialoro condensation of *p*-hydroxybenzaldehyde. Both isomers have now been obtained by diazotisation of the respective *p*-amino-acids and decomposition of the diazonium salts. The *cis*- and the *trans*-α-hydroxy-acids have the same m. p. and give no depression on admixture; conversion of one into the other, probably *cis* into *trans*, takes place on heating and is complete before the m. p. is reached. This resembles the conversion of *cis*- into *trans*-*p*-methoxystilbene by heat noted by Kon and Spickett (*loc. cit.*). That the two compounds are different is proved by methylation to *cis*- and *trans*-methoxy-acids of widely different m. p. Owing to the transformation it is impossible to say from the m. p. alone which isomer Zincke and Geibel (*loc. cit.*) prepared. The *p*-hydroxy-acid obtained from *p*-hydroxybenzaldehyde by their method, namely condensation, must be *trans* as it is found to give a methoxy-acid, which does not depress the m. p. of the *trans*-*p*-methoxy-acid prepared from the *trans*-*p*-hydroxy-acid derived from the *trans*-nitro-acid. Both the *trans*- (Oglialoro, *Jahresber. Fortsch. Chem.*, 1879, 731) and the *cis*-*p*-methoxy-acid (Stoermer and Prigge, *Annalen*, 1915, **409**, 20) were previously obtained respectively by condensation from *p*-anisaldehyde and by ultraviolet irradiation of the *trans*-isomer.

Discussion.—Apart from the *o*-nitro- and the *o*-amino-acid already fully substantiated, all the *cis*- and *trans*-aryl-α-phenylcinnamic acids *ortho*-, *meta*-, and *para*-substituted with the groups under consideration have thus been examined (insofar as they can exist as free acids), and their stereochemical configurations have been settled. It is seen from the Table that most, but not all, of the *trans*- melt higher than the corresponding *cis*-isomers. This property cannot, therefore, be used safely for allocation of configuration. Fractional precipitation used in separations shows that the *cis*-acids are the stronger in the nitro-series and probably throughout. The main, and usually the sole, products of the Perkin–Oglialoro condensation are now proved to have the *trans*-configuration.

When benzaldehyde and phenylacetic anhydride condense, the initial product can have either the (±)-configuration (VIII*a*; A = acyl) or the isomeric (±)-form (IX*a*). No free hydroxyl groups are to be expected in the presence of acid anhydride at high temperatures. If the sterically effective bulk of the groups is assumed to be in the order

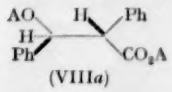
Ph > OA > H and Ph > CO_2A > H the configuration (VIII*a*) involves less steric compression than the alternative (IX*a*) and is consequently likely to be formed in preference. Once formed, the intermediate loses HOA by elimination. This takes place most readily (Barton, *J.*, 1953, 1029) when the four centres concerned lie in one plane, as in the alternative conformations (VIII*b*) and (IX*b*). Elimination from (VIII*b*) will clearly lead to

Melting points of aryl-α-phenylcinnamic acids.

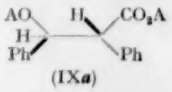
		NO_2	NH_2	OH	OMe	H	
ortho	*cis*	147° *	—	—	131·5°		
	trans	197 *	186°	195°	184		
meta	*cis*	196 †	190	134	86	*cis*	137°
	trans	184 †	192	187	195	*trans*	172
para	*cis*	143 (127)	221	(222)	123		
	trans	217	213 (208)	223	192		

* Bakunin, *loc. cit.*; Pschorr, *Ber.*, 1896, **29**, 496; Stoermer and Prigge, *loc. cit.*
† Bakunin, *loc. cit.*

trans- and from (IX*b*) to *cis*-α-phenylcinnamic acid. The formation of the *trans*-acids in practice, therefore, indicates that steric factors in the intermediate state are the determining factor. The formation of 3-phenylcoumarin, the lactone of the *cis*-acid, when salicylaldehyde is condensed is an exception: it has been shown (Crawford and Shaw, *J.*, 1953, 3435) to be due to interaction between groups OA in the ring and CO_2A before the elimination stage. Another exception, namely, the formation of small amounts of *cis*-nitro-acids, is more difficult to account for. Taylor and Hobson (*J.*, 1936, 181) have suggested that the stability of *cis*-*o*-nitrostilbene is due to the attraction between one phenyl group and the nitro-group attached to the other. Such an attraction in these condensations would overcome to some extent the steric repulsion between the bulky aryl groups resulting in the formation of some intermediate corresponding to (IX). The formation of *cis*-acids is being studied at present.

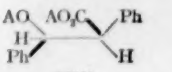


(VIII*a*)



(IX*a*)

(VIII*b*)



(IX*b*)

Experimental

trans-o-*Hydroxy-α-phenylcinnamic Acid.*—3-Phenylcoumarin (7·5 g.) in 6% sodium hydroxide solution (50 ml.) was refluxed for 4 hr. with yellow mercuric oxide (20 g.) and water (400 ml.). Addition of dilute acetic acid precipitated a mercury compound which was filtered off and boiled for 30 min. with concentrated hydrochloric acid (3 ml.), water (300 ml.), and alcohol (50 ml.). The solution, filtered cold and boiled to remove alcohol, deposited *trans*-*o*-hydroxy-α-phenylcinnamic acid (0·5 g.), colourless needles (from benzene), m. p. 195° (Found: C, 75·8; H, 5·3. $C_{15}H_{12}O_3$ requires C, 75·1; H, 5·0%).

trans-o-*Methoxy-α-phenylcinnamic Acid.*—*Method A.* The foregoing hydroxy-acid (0·2 g.) with methyl sulphate and potassium hydroxide gave the methoxy-acid (0·15 g.), cream plates (from benzene), m. p. 184°. *Method B.* Perkin–Oglialoro condensation of *o*-methoxybenzaldehyde (9 g.) gave the methoxy-acid (2 g.), colourless needles (from alcohol), m. p. 183° undepressed by the previous product. This *trans*-acid was readily converted into 3-phenylcoumarin by 20 minutes' refluxing with pyridine hydrochloride.

cis-o-*Methoxy-α-phenylcinnamic Acid.*—3-Phenylcoumarin (3·1 g.) in water (40 ml.) containing potassium hydroxide (6 g.) was refluxed for 1 hr. with methyl sulphate (6·2 ml.) and then for another 2 hr. after the addition of 50% potassium hydroxide solution (10 ml.). When the product was poured on ice and hydrochloric acid and suitably extracted, the cis-*acid* (1·1 g.)

was obtained; it formed colourless prisms, m. p. 131·5°, from benzene (Found: C, 76·0; H, 5·5. $C_{16}H_{14}O_3$ requires C, 75·6; H, 5·5%).

Configuration of the Isomeric m-*Nitro- and* m-*Amino-α-phenylcinnamic Acids.*—The nitro-acids were prepared according to Bakunin (*loc. cit.*) from *m*-nitrobenzaldehyde (16 g.) (yields: acid of m. p. 184°, 7 g.; acid of m. p. 196°, 3·5 g.). The acid of m. p. 184° was reduced with ferrous sulphate and ammonia to the amino-acid, m. p. 192°, in 57% yield. This (3 g.) on diazotisation and reduction with hypophosphorous acid gave *trans*-α-phenylcinnamic acid (1·1 g.), m. p. 167—168°, not depressed on admixture with a genuine sample of m. p. 171°. The second nitro-acid on reduction gave a 40% yield of the amino-acid, m. p. 190—191°, which (1·5 g.) in turn gave *cis*-α-phenylcinnamic acid (0·55 g.), m. p. 133° alone or mixed with a genuine sample of m. p. 135°.

trans-m-*Hydroxy-α-phenylcinnamic Acid.*—*Method A.* Perkin–Oglialoro condensation of *m*-hydroxybenzaldehyde (9 g.) gave the hydroxy-acid (13·5 g.) as straw-coloured needles, m. p. 183—184° (from alcohol). *Method B.* Decomposition of the diazonium salt from *trans-m*-amino-α-phenylcinnamic acid (15 g.) gave the acid (5 g.) as light brown needles (from benzene), m. p. 187°, not depressing the m. p. of the foregoing product. Methylation of this acid (2·2 g.) gave the *trans*-methoxy-acid (1·8 g.), colourless needles (from alcohol), m. p. 195°.

cis-m-*Hydroxy-α-phenylcinnamic Acid.*—Diazotisation and decomposition of the *cis-m*-amino-acid (2·5 g.) gave the cis-m-*hydroxy-acid* (0·75 g.), fine colourless needles (from benzene), m. p. 134° (Found: C, 74·6; H, 4·9%). Methylation gave cis-m-*methoxy-α-phenylcinnamic acid* (0·4 g.), colourless needles (from benzene), m. p. 86° (Found: C, 75·7; H, 5·6%).

cis- *and* trans-p-*Nitro-α-phenylcinnamic Acid.*—Bakunin's method (*loc. cit.*) gave, from *p*-nitrobenzaldehyde (30 g.), a nitro-acid of m. p. 217° (18 g.), believed to be *trans*, and one of m. p. 143° (5 g.).

trans-p-*Amino-α-phenylcinnamic Acid.*—Reduction of the *p*-nitro-acid of m. p. 217° (10 g.) with ferrous sulphate and ammonia gave the *amino-acid* (6 g.), mustard-coloured needles (from alcohol), m. p. 213° (Found: C, 74·8; H, 5·5; N, 6·0. $C_{15}H_{13}O_2N$ requires C, 75·3; H, 5·5; N, 5·9%). A form of this acid melting at 208° was obtained on subsequent occasions. The *trans*-configuration was established by diazotisation and reduction to *trans*-α-phenylcinnamic acid, m. p. and mixed m. p. 172°.

trans-p-*Hydroxy-α-phenylcinnamic Acid.*—*Method A.* Perkin–Oglialoro condensation of *p*-hydroxybenzaldehyde (10 g.) gave the acid (16·5 g.), colourless needles (from alcohol), m. p. 223°. *Method B.* Decomposition of the remarkably stable diazonium salt from the foregoing amino-acid (9·3 g.) gave the hydroxy-acid (6 g.), m. p. 222°, not depressed by the foregoing product, but this is not proof of identity in this case. Addition of the methyl ether of the second product (colourless needles, m. p. 190°) did not depress the m. p. of the methyl ether of the first product (m. p. 188°).

cis-p-*Amino-α-phenylcinnamic Acid.*—Reduction of the *p*-nitro-acid of m. p. 143° (12 g.) gave two amino-acids. The cis-*acid* (4·5 g.), less soluble and hence first to separate, had m. p. 220°, cream-coloured needles (from alcohol) (Found: C, 74·9; H, 5·3; N, 5·85%). The more soluble acid (3·6 g.), m. p. 206°, did not depress the m. p. of *trans-p*-amino-α-phenylcinnamic acid. The less soluble acid (1·1 g.) on diazotisation and reduction gave *cis*-α-phenylcinnamic acid (0·35 g.), m. p. and mixed m. p. 133°. Irradiation of the *trans-p*-amino-acid (20 g. in 600 ml. of alcohol) in a quartz flask with ultraviolet light for 50 hr. gave the *cis*-acid (6·4 g.), m. p. 221°, which separated from solution during the irradiation. Diazotisation of this acid and treatment with cupro-cupri-sulphite reagent and sodium nitrite solution (*Org. Synth.*, 1948, **28**, 52) gave *cis-p*-nitro-α-phenylcinnamic acid, m. p. 127° (but 143° on remelting). Reduction of this nitro-acid gave only *trans-p*-amino-α-phenylcinnamic acid, m. p. 208°, confirmed by a mixed m. p. and high solubility.

cis-p-*Hydroxy-α-phenylcinnamic Acid.*—Decomposition of the very stable diazonium salt of the *cis-p*-amino-acid (2 g.) gave the *hydroxy-acid* (1 g.), m. p. 222°, long colourless needles from alcohol (Found: C, 75·1; H, 5·0%). Addition of this acid did not depress the m. p. of the *trans*-acid. Methylation gave the *cis-p*-methoxy acid, m. p. 123°, colourless needles from alcohol.

College of Technology, Belfast. [*Received, April 21st*, 1955.]

The Synthesis and Antibacterial Activity of Some Basic Derivatives of the Bile Acids.

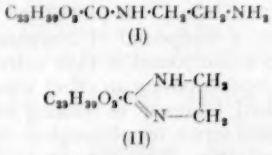
By Marjorie L. Hilton, A. S. Jones, and J. R. B. Westwood.

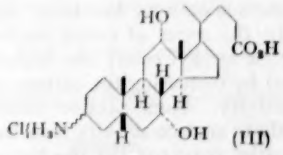
[Reprint Order No. 6402.]

Two series of basic derivatives of the bile acids have been synthesised, the first by the reaction of the methyl esters of certain bile acid derivatives with ethylenediamine hydrate and the second by esterification of 3-amino-7α : 12α-dihydroxycholanoic acid hydrochloride with a number of alcohols. The bacteriostatic activity of the compounds against *Staphylococcus aureus* and *Aerobacter aerogenes*, and their ability to depress the surface tension of the culture media of these organisms, showed no relation between the two properties for the ethylenediamine derivatives, but revealed a striking parallelism for the second set of esters.

Stacey and Webb (*Proc. Roy. Soc.*, 1947, *B*, **134**, 523) showed that the antibacterial activity of certain anionic bile acid derivatives depended on their surface activity: the depression of the surface tension of the culture medium by these compounds at their limiting bacteriostatic concentration for *Staphylococcus aureus* was in every case approximately 4·5 dynes/cm. No such relation existed, however, for a series of cationic bile acid derivatives (Stacey and Webb, *ibid.*, p. 538). The anionic derivatives used in these investigations had closely related structures in that they all contained a carboxyl group in the bile acid side chain. The cationic derivatives, however, varied in that some contained amino-, amidino-, and guanidino-groups in the bile acid side chain, while others contained amino-groups in the nucleus. It appeared desirable, therefore, to study more closely related compounds. Methods were sought for producing such compounds without resorting to the tedious production of 23- and 24-amino-derivatives (James, Smith, Stacey, and Webb, *J.*, 1946, **665**; Hilton and Webb, *J.*, 1951, 2767).

First, methyl esters of certain bile acid derivatives were treated with boiling ethylenediamine hydrate, giving the required basic derivatives in one step. Methyl cholate thus gave *N*-3α : 7α : 12α-trihydroxycholanoylethylenediamine. From the analytical data and the fact that the compound reacted as a primary and not as a secondary amine (Feigl and Anger, *Mikrochim. Acta*, 1937, **1**, 138) it was considered to have the open-chain structure (I) and not the ring form (II) which would result by loss of water (cf. Hill and Aspinall, *J. Amer. Chem. Soc.*, 1939, **61**, 822; Aspinall, *ibid.*, p. 3195). Methyl deoxycholate, lithocholate, apocholate, 3α : 12α-dihydroxychol-14-enoate, and 3-amino-7α : 12α-dihydroxycholanoate hydrochloride gave similar products; with the unsaturated derivatives there was the possibility of migration of the double bond, but its position in the final product was not ascertained.





A second method was simply to esterify 3-amino-7α : 12α-dihydroxycholanoic acid hydrochloride (III) (Jones, Webb, and Smith, *J.*, 1949, 2164) with a number of straight-chain and branched-chain alcohols. (Syntheses of the methyl and *iso*pentyl esters have already been reported; Jones, Webb, and Smith, *loc. cit.*)

These compounds were tested for antibacterial activity against *Staph. aureus* and *Aerobacter aerogenes* and for their ability to depress the surface tension of the culture media of these organisms.

It was apparent (Tables 2 and 3) that there was no close relation between the bacteriostatic activities and surface activities of the ethylenediamine derivatives. Thus, at the

limiting dilution which was bacteriostatic for *Staph. aureus* the depression of surface tension varied from 6·0 dynes/cm. for *N*-3α : 7α : 12α-trihydroxycholanoylethylenediamine to 2·5 dynes/cm. for *N*-3α-hydroxycholanoylethylenediamine. Moreover, the compounds with the highest surface activity did not show the highest bacteriostatic activity. There did appear to be, however, a relation between the bacteriostatic activity and surface activity of the esters of 3-amino-7α : 12α-dihydroxycholanoic acid hydrochloride. Thus, as the carbon chain was increased, the antibacterial activities of the compounds increased in the same order as their surface activities, both rising to a maximum at the *n*-hexyl and *iso*pentyl esters and, for eight of the twelve esters studied, the values for the depression of the surface tension at the limiting dilution which was bacteriostatic for *Staph. aureus* were between 13·2 and 11·2 dynes/cm. (mean = 12·2; $\sigma \pm 0{\cdot}9$). It may be noted that the limiting dilutions varied from 1 : 256,000 for the *n*-hexyl ester (depression 13·2 dynes/cm.) to 1 : 8000 for the *n*-propyl ester (depression 13·2 dynes/cm.).

Similar results were obtained by Birchenough (*J.*, 1951, 1263) for a series of 2-alkylpyridinium salts in which maximum antibacterial action and maximum depression of surface tension occurred when the alkyl group was *n*-pentadecyl.

In considering these and other results Burton (*Sci. Prog.*, 1951, **39**, 253) pointed out that there was some correlation between antibacterial activity and surface activity in a homologous series of quaternary ammonium compounds, but that there was none between compounds of different series. He concluded that the antibacterial action of quaternary ammonium compounds depended partly on their specific structure and partly on surface activity, the latter effect predominating in a homologous series. The results obtained here with the esters of 3-amino-7α : 12α-dihydroxycholanoic acid may be explained on the same basis, the effect of surface activity predominating with the long-chain esters, but that due to specific structure predominating with the methyl and ethyl esters, both of which showed comparatively low surface activity at their limiting bacteriostatic concentrations (depression, 8·0 and 7·8 dynes/cm. respectively).

The *iso*hexyl and 2-ethylhexyl esters showed lower bacteriostatic activities than would be expected from their surface activities. This may have been due to the fact that at the limiting bacteriostatic concentrations these compounds formed a thick emulsion with the constituents of the culture medium, which may have interfered with determination of the surface tensions. A similar effect occurred at the limiting dilutions which were bacteriostatic for *Aerobacter aerogenes*, with many of the less active compounds, so no definite conclusions could be reached in this case. It may be noted, however, that for the more active derivatives, again with the exception of the ethyl ester, the depression of surface tension at the limiting bacteriostatic dilution varied only from 13·2 to 14·3 dynes/cm.

It appears from the high antibacterial activity of 23-amino-3α-hydroxynorcholane hydrochloride and many other basic bile acid derivatives (Stacey and Webb, *Proc. Roy. Soc.*, 1947, *B*, **134**, 538; Hilton and Webb, *J.*, 1951, 2767), compared with their low surface activity, that, in general, the bacteriostatic activity of the basic bile acid derivatives is not due to surface activity but to a "specific-structure effect" as postulated by Burton (*loc. cit.*). In the series of esters studied, however, a compound of comparatively low activity (*e.g.*, a methyl ester) was transformed into a compound of high activity (*e.g.*, a *n*-hexyl ester) by increasing the carbon chain, thus superimposing an effect which was due to surface activity. Some caution should be exercised, however, in relating antibacterial power directly to surface activity even in a homologous series, for although in such a series surface activities may parallel the bacteriostatic activities, there remains the possibility that both properties may be dependent upon a third and more fundamental variable.

Experimental

N-3α : 7α : 12α-*Trihydroxycholanoylethylenediamine Hydrochloride.*—A solution of methyl cholate (0·5 g.) in ethylenediamine hydrate (10 ml.) was boiled under reflux for 3 hr. The cooled solution was poured into water (200 ml.) and made strongly alkaline with 5N-sodium hydroxide, and the precipitated base filtered off after 18 hr. and dried *in vacuo* (P_2O_5–NaOH). Addition of 5N-hydrochloric acid to a suspension of the base in acetone, followed by the addition

of excess of acetone, precipitated N-3α : 7α : 12α-*trihydroxycholanoylethylenediamine hydrochloride* (0·1 g.), which crystallised from aqueous acetone as needles, m. p. 275° (sintering at 250°), $[\alpha]_D^{18}$ +37·6° (*c*, 0·94 in H_2O) (Found, after drying at 190°: C, 64·1; H, 9·6; N, 5·8. $C_{26}H_{46}O_4N_2$,HCl requires C, 64·1; H, 9·7; N, 5·8%).

N-3α : 12α-*Dihydroxycholanoylethylenediamine Hydrochloride.*—Methyl deoxycholate (1 g.) and ethylenediamine hydrate (10 ml.) were boiled under reflux for 3 hr. The solution was evaporated under reduced pressure and the crystalline residue dried *in vacuo* (H_2SO_4) and dissolved in chloroform (30 ml.). Dry hydrogen chloride was bubbled through this solution at 0° until no further precipitation was apparent. The supernatant solution was removed and the precipitate triturated with acetone until solid. Crystallisation from aqueous acetone gave N-3α : 7α-*dihydroxycholanoylethylenediamine hydrochloride* (300 mg.), needles, m. p. 177—178°, $[\alpha]_D^{20}$ +34·6° (*c*, 1·04 in H_2O) (Found, after drying at 160°: C, 65·9; H, 9·6; N, 6·3. $C_{26}H_{46}O_3N_2$,HCl requires C, 66·3; H, 10·0; N, 5·95%).

N-3α-*Hydroxycholanoylethylenediamine Hydrochloride.*—Methyl lithocholate (0·2 g.) in ethylenediamine hydrate was boiled under reflux for 3 hr. The gelatinous material obtained upon cooling was triturated with water until a granular solid was produced which was then suspended in water (100 ml.) and made alkaline to litmus with 5N-sodium hydroxide. The solid material was filtered off, washed with water, dried, and dissolved in acetone–ethanol (2 : 1) containing a few drops of 5N-hydrochloric acid. Addition of excess of acetone to the filtered solution precipitated a gelatinous solid which was dissolved in ethanol, and the solution evaporated under reduced pressure. Trituration of the resulting syrup with acetone–ethanol (4 : 1) gave crystals which, recrystallised from aqueous acetone, gave N-3α-*hydroxycholanoylethylenediamine hydrochloride* (75 mg.) as needles, m. p. 193—195° (sintering at 175°), $[\alpha]_D^{19}$ +16° (*c*, 1·0 in EtOH) (Found, after drying at 170°: N, 6·3. $C_{26}H_{46}O_2N_2$,HCl requires N, 6·2%).

Methyl *apo*cholate (1 g.) (Boedecker, *Ber.*, 1920, **53**, 1852; 1921, **54**, 2489; 1922, **55**, 2302) and methyl 3α : 12α-dihydroxychol-14(15)-enoate (100 mg.) (Boedecker, *loc. cit.*, 1921) were treated with ethylenediamine hydrate as described above and the products isolated essentially by the method used for the methyl deoxycholate product. N-3α : 12α-*Dihydroxychol*-8(14)-*enoyl*- (175 mg.), m. p. 145° (decomp.), $[\alpha]_D^{20}$ +26° (*c*, 1·0 in H_2O) (Found, after drying at 120°: C, 66·4; H, 9·7; N, 5·5. $C_{16}H_{44}O_3N_2$,HCl requires C, 66·6; H, 9·6; N, 6·0%), and N-3α : 12α-*dihydroxychol*-14(15)-*enoyl-ethylenediamine hydrochloride* (60 mg.), m. p. 148° (decomp.), $[\alpha]_D^{20}$ +37·4° (*c*, 1·01 in H_2O) (Found, after drying at 120°: C, 66·2; H, 9·6; N, 6·0%), were isolated (absence of migration of the double bonds being assumed).

N-3-*Amino*-7α : 12α-*dihydroxycholanoylethylenediamine Dihydrochloride.*—A solution of methyl 3-amino-7α : 12α-dihydroxycholanoate hydrochloride (400 mg.) in ethylenediamine hydrate (3 ml.) was boiled under reflux for 3 hr. The cooled solution was made strongly alkaline by 5N-sodium hydroxide, the product separating as an oil. The oil was centrifuged, the supernatant liquid removed, and the sediment dried *in vacuo* (P_2O_5–H_2SO_4). The dried material was then dissolved in ethanol, and the hydrochloride formed by the addition of 5N-hydrochloric acid. Sodium chloride, which was precipitated, was filtered off and the ethanol solution evaporated to dryness. Crystallisation of the solid residue from aqueous acetone gave N-3-*amino*-7α : 12α-*dihydroxycholanoylethylenediamine dihydrochloride* (245 mg.) as needles, m. p. 260° (decomp.), $[\alpha]_D^{20}$ +44° (*c*, 1·0 in H_2O) (Found, after drying at 190°: N, 7·9. $C_{26}H_{47}O_3N_3$,2HCl requires N, 8·0%).

Esters of 3-*Amino*-7α : 12α-*dihydroxycholanic Acid Hydrochloride.*—The hydrochloride

TABLE 1. *Alkyl* 3-*amino*-7α : 12α-*dihydroxycholanoate hydrochlorides.*

		Found (%)				Required (%)		
Alkyl	Decomp.	C	H	N	Formula	C	H	N
Me	250°	65·6	9·8	3·15	$C_{25}H_{43}O_4N$,HCl	65·6	9·8	3·1
Et	260—270	66·6	9·6	3·0	$C_{26}H_{45}O_4N$,HCl	66·1	10·0	3·0
Pr^n	235	64·6	9·8	2·8	$C_{27}H_{47}O_4N$,HCl,H_2O	64·6	10·1	2·8
Bu^n	250	65·4	9·6	2·7	$C_{28}H_{49}O_4N$,HCl,H_2O	65·0	10·2	2·7
n-C_5H_{11}	250	65·6	10·2	2·8	$C_{29}H_{51}O_4N$,HCl,H_2O	65·5	10·3	2·65
n-C_6H_{11}	260	65·9	10·3	2·5	$C_{30}H_{53}O_4N$,HCl,H_2O	66·1	10·5	2·6
n-C_6H_{17}	270	67·5	10·7	2·2	$C_{33}H_{57}O_4N$,HCl,H_2O	67·0	10·6	2·4
Pr^i	270	66·6	10·1	3·0	$C_{27}H_{47}O_4N$,HCl	66·7	10·1	2·9
Bu^i	235	67·0	10·2	2·7	$C_{28}H_{49}O_4N$,HCl	67·3	10·2	2·8
CH_2Bu^i	260—270	65·3	10·5	2·7	$C_{29}H_{51}O_4N$,HCl,H_2O	65·5	10·3	2·65
$CH_2{\cdot}CH_2Bu^i$	250	67·5	10·4	2·85	$C_{30}H_{53}O_4N$,HCl	68·3	10·4	2·65
$Bu^n{\cdot}CHEt{\cdot}CH_2$	250	67·3	10·7	2·5	$C_{33}H_{57}O_4N$,HCl,H_2O	67·0	10·6	2·4

TABLE 2. *The bacteriostatic activities of some basic bile acid derivatives.*

No.	Hydrochloride of	Limiting bacteriostatic dilution against: *Staph. aureus* 16 hr. at 37°	*Staph. aureus* 40 hr. at 37°	*Aerobact. aerogenes* 16 hr. at 37°	*Aerobact. aerogenes* 40 hr. at 37°
1	23-Aminonorcholan-3α-ol	256,000	256,000	Inactive	Inactive
2	23-Aminonorcholan-3-one	64,000	64,000	Inactive	Inactive
	Ethylenediamine derivatives				
3	*N*-3α : 7α : 12α-Trihydroxycholanoyl-	8000	8000	2000	2000
4	*N*-3α : 12α-Dihydroxycholanoyl-	32,000	32,000	16,000	16,000
5	*N*-3α-Hydroxycholanoyl-	32,000	16,000	—	—
6	*N*-3α : 12α-Dihydroxychol-8(14)-enoyl-	16,000	16,000	4000	4000
7	*N*-3α : 12α-Dihydroxychol-14(15)-enoyl-	32,000	16,000	4000	2000
8	*N*-3-Amino-7α-12α-dihydroxycholanoyl- (dihydrochloride)	32,000	16,000	Inactive	Inactive
	Esters of 3-amino-7α : 12α-dihydroxycholanoic acid				
9	Methyl	8000	8000	2000	2000
10	Ethyl	16,000	16,000	4000	4000
11	*n*-Propyl	16,000	8000	16,000	8000
12	*n*-Butyl	64,000	32,000	8,000	8000
13	*n*-Pentyl	128,000	128,000	32,000	8000
14	*n*-Hexyl	256,000	256,000	4000	2000
15	*n*-Octyl	128,000	32,000	Inactive	Inactive
16	*iso*Propyl	16,000	16,000	8000	8000
17	*iso*Butyl	32,000	32,000	32,000	16,000
18	*iso*Pentyl	64,000	64,000	32,000	16,000
19	*iso*Hexyl-	8000	4000	Inactive	Inactive
20	2-Ethylhexyl	2000	2000	Inactive	Inactive

TABLE 3. *Depression of the surface tension (dynes/cm.) of nutrient-broth medium.*

No.	Dilution, 1 in.: 2000	4000	8000	16,000	32,000	64,000	128,000	256,000	512,000
1	—	—	—	—	2·7	2·1	1·0	<1	—
2	—	—	—	3·1	1·8	1·1	0·5	—	—
3	8·9	8·7	6·0	4·2	3·3	—	—	—	—
4	—	—	—	5·1	4·2	2·9	2·4	—	—
5	—	—	—	2·5	1·9	1·9	1·6	—	—
6	—	7·1	6·2	5·6	3·2	2·1	1·2	—	—
7	6·5	5·1	4·2	3·3	2·6	2·0	1·4	—	—
8	—	—	3·1	2·5	2·3	1·3	0·5	—	—
9	—	9·6	8·0	6·8	6·3	—	—	—	—
10	—	10·7	8·7	7·8	7·0	6·6	—	—	—
11	—	—	13·2	9·9	10·6	7·0	—	—	—
12	—	—	13·7	12·5	12·2	10·8	8·8	—	—
13	—	—	14·2	16·3	15·5	14·2	11·2	9·3	—
14	—	17·4	18·0	18·0	—	17·1	16·3	13·2	10·7
15	—	—	—	14·5	13·1	12·8	8·0	6·3	4·3
16	—	—	13·7	11·5	10·9	8·2	—	—	—
17	—	—	—	14·2	11·2	8·8	7·7	—	—
18	—	—	—	14·3	13·2	11·6	7·9	—	—
19	—	16·1	14·8	13·6	10·6	—	—	—	—
20	17·5	16·8	15·5	10·5	—	—	—	—	—

At limiting dilution bacteriostatic (after 40 hr.) for:

No.	*Staph. aureus*	*Aerobact. aerogenes*	No.	*Staph. aureus*	*Aerobact. aerogenes*
1	<1	Inactive	11	13·2	13·2
2	1·1	Inactive	12	12·2	13·7
3	6·0	8·9	13	11·2	14·2
4	4·2	5·1	14	13·2	—
5	2·5	—	15	13·1	Inactive
6	5·6	7·1	16	11·5	13·7
7	3·3	5·1	17	11·2	14·2
8	2·5	Inactive	18	11·6	14·3
9	8·0	—	19	16·1	Inactive
10	7·8	10·7	20	17·5	Inactive

(Jones, Webb, and Smith, *J.*, 1949, 2164) was heated on a boiling-water bath with the appropriate alcohol, either containing 20% of dry hydrogen chloride or mixed with 8% of 10N-hydrochloric acid. The solvents were removed by distillation or steam-distillation under reduced pressure. The syrupy *ester hydrochlorides* solidified on trituration with acetone. They crystallised and were recrystallised from ethanol–acetone (1 : 4) or water (see Table 1). Analyses were of samples dried at 60° under reduced pressure: some of the esters then still retained water of crystallisation.

Determination of Bacteriostatic Activity.—The bacteriostatic activities of the various derivatives against *Staphylococcus aureus* and *Aerobacter aerogenes* were determined by the serial-dilution method in a nutrient broth of the following composition: Lab. Lemco 1%, Oxoid bacteriological peptone 1%, and sodium chloride 0·5% (adjusted to pH 7).

Tubes of media containing suitable concentrations of the bile acid derivatives were sterilised for 30 min. at 15 lb./sq. in., cooled, and inoculated from a sterile pipette with one drop of a 24 hr. culture of the organism in nutrient broth. After a suitable time, the inhibition of growth of the organism was measured by comparison with the control. Determinations were in duplicate and are recorded in Table 2. The activities of 23-aminonorcholan-3α-ol hydrochloride and 23-aminonorcholan-3-one hydrochloride (Hilton and Webb, *loc. cit.*) are included for comparison.

Determination of Surface Activity.—The depression of the surface tension of the nutrient-broth medium was determined over a range of concentrations. Surface tension was measured with the du Nöuy tensiometer on 5 ml. of the solution 2 minutes after the formation of the surface (this time was important for reproducibility; see Gaddum, *Proc. Roy. Soc.*, 1931, *B*, 109, 114). These results are recorded in Table 3.

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The Cryoscopic Behaviour of Polynitro-compounds in Sulphuric Acid.

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The effects are reported of various additional solutes upon the molecular depressions of picric acid, 1 : 3 : 5-trinitrobenzene, and 2 : 4 : 6-trinitrotoluene in sulphuric acid. The value of θ/m_2 varies more or less with the concentration (m_2) of the polynitro-compound and with the concentration (m_3) of the third component, but is in general (for $m_2 \sim 0{\cdot}04$) greater than the cryoscopic constant (K_f) with water and less than K_f with potassium hydrogen sulphate, ammonium hydrogen sulphate, or disulphuric acid as third component. Nitromethane differs from the polynitro-compounds in giving θ/m_2 greater than K_f in the presence of potassium hydrogen sulphate. A comparison is drawn between the behaviour of the polynitro-compounds and the variations in the solubility of sulphur dioxide near 100% sulphuric acid.

THE form in which aromatic polynitro-compounds exist in solution in anhydrous sulphuric acid has been a matter of some controversy. Since results of reasonable precision have been obtainable by the cryoscopic technique, Hammett and Deyrup (*J. Amer. Chem. Soc.*, 1933, 55, 1900) have regarded picric acid and 1 : 3 : 5-trinitrobenzene as non-electrolytes, Gillespie (*J.*, 1950, 2542; 1954, 1851) has attributed deviations of the order of 10% from the ideal molecular depression for a non-electrolyte to some basic character in 2 : 4 : 6-trinitrotoluene, and Brand, Horning, and Thornley (*J.*, 1952, 1374) could find no spectrophotometric evidence at all for the ionisation of this compound in 100% sulphuric acid. One of us (Wyatt, *J.*, 1953, 1175) attempted to reconcile the conflicting spectrophotometric and cryoscopic evidence for 2 : 4 : 6-trinitrotoluene by reference to the variability in the cryoscopic constant (K_f) to be expected from a dissociating solvent when the extent of dissociation is altered; but the K_f values deduced were at variance with the simple theory

developed and disagreed with Kunzler and Giauque's calorimetric measurements (*J. Amer. Chem. Soc.*, 1952, **74**, 3472). A possible alternative explanation in terms of salt effects has therefore been proposed (Wyatt, *J.*, 1954, 2647).

In the work now reported, an investigation has been made of the molecular depressions of freezing-point caused by polynitro-compounds and nitromethane in the presence of potassium hydrogen sulphate and other solutes which interfere with the solvent dissociation. It appears that the suggestion that bases which suppress the solvent dissociation may be used indiscriminately in the cryoscopic method (Gillespie, Hughes, and Ingold, *J.*, 1950, 2473, see p. 2484) can be misleading, at least in the case of solutes which ionise hardly, if at all (*i.e.*, $\nu \sim 1$). In such cases even qualitative conclusions about basic strength are unreliable when founded upon molecular depressions in the presence of one only of the many solutes which could be used to reduce the solvent dissociation. Until the detailed behaviour of the polynitro-compounds has received an adequate, quantitative explanation no arbitrary selection of the cryoscopic data can justifiably be held to be in conflict with the spectrophotometric interpretation of these compounds as non-electrolytes.

Experimental

The experimental arrangements followed closely those recommended by Gillespie, Hughes, and Ingold (*loc. cit.*), except that a 6—11° solid-stem mercury-in-glass thermometer graduated in 0·01° was used (Gillespie and Leisten, *J.*, 1954, 1) and that a single-armed stirrer operated by one solenoid was found to be adequate for stirring the contents of the cryoscope. In some preliminary experiments attempts were made to use thermistors for temperature measurements (cf. Gold, Hawes, and Tye, *J.*, 1952, 2167), but with 2 volts across a bridge with 6000 ohms in each arm the readings were not reliable even to 0·01°; and, although improvements might have been possible by reducing the potential a more elaborate galvanometer system would then have been necessary for detection.

Materials.—The oleum and slightly aqueous solutions of sulphuric acid were prepared in the usual manner (Gillespie, Hughes, and Ingold, *loc. cit.*) and the molality of excess of water or disulphuric acid was estimated from the freezing-point. Potassium sulphate and ammonium sulphate of "AnalaR" quality were dried for 2 hr. at 105°. Commercial 1 : 3 : 5-trinitrobenzene and picric acid were twice recrystallised from glacial acetic acid or methylated spirits respectively and dried at 100°. Commercial 2 : 4 : 6-trinitrotoluene was recrystallised three times from chloroform, dried between filter-papers, and kept for two days in a vacuum-desiccator. Nitromethane was dried ($CaCl_2$) and distilled just before use. Technical acetone was purified by means of the sodium iodide addition compound (Shipsey and Werner, *J.*, 1913, **103**, 1255), dried (K_2CO_3), and distilled.

Results.—The results are collected in Tables 1—4, in which m_2 indicates the molality of the nitro-compound and $(\theta/m_2)'$ gives the value of the molecular depression corrected slightly as described below. θ represents the depression of freezing-point from that of the solvent after treatment with the third component, the concentration of which was so arranged that the initial freezing-point was roughly 9·5°, 8·5°, or 7·5°. Variations in the molecular depression due to the usual inperfections in the simple cryoscopic formula were allowed for by a correction term similar to that of Hammett and Deyrup (*loc. cit.*) and Gillespie, Hughes, and Ingold, (*loc. cit.*). To simplify the presentation here, all molalities in the Tables were calculated from the solvent weight *after* allowance for reaction to form solutes of the types $M^+HSO_4^-$ and $H_2S_2O_7$ with the third component, and possible solvation of any particles present was ignored. The relationship between the corrected, $(\theta/m_2)'$, and the observed molecular depression, $(\theta/m_2)_{obs.}$, is

$$(\theta/m_2)' = (\theta/m_2)_{obs.}\{1 + 0{\cdot}00350 + (\overline{m}_2 + 2m_3)/m_1\}$$

where the symbols in the correction term have the same significance as in Gillespie's formula. The correction term does not affect the general trend of the results, being usually less than 1·03, and it has not been applied in the case of disulphuric acid solution in view of the uncertainties in ν_3 and s_3 due to the possible formation of higher polyacids (Gillespie, *loc. cit.*, p. 2516). Since 2 : 4 : 6-trinitrotoluene solutions slowly reddened on exposure to sunlight, the cryoscope was exposed to ultraviolet radiation from a high-pressure quartz-mercury arc after the final addition of the trinitrotoluene in the runs quoted in Tables 3*a* and 3*b*, and any possible variation in the freezing-point sought. After 2 hr. the final freezing-point of 7·816° quoted in Table 3*a* had

TABLE 1. *Molecular depressions of picric acid.*

(*a*) Molality of $(H_3O^+ \cdot HSO_4^-) = 0.093$

m_2	—	0.0223	0.0459	0.0929	0.1612
F. p.	... 9.511°	9.368°	9.221°	8.945°	8.563°
$(\theta/m_2)'$	—	6.55	6.45	6.26	6.06

(*b*) Molality of $(H_3O^+ \cdot HSO_4^-) = 0.173$

—	0.0186	0.0410	0.0856	0.1562
8.643°	8.531°	8.395°	8.136°	7.732°
—	6.21	6.30	6.19	6.12

(*c*) Molality of $(H_3O^+ \cdot HSO_4^-) = 0.298$

m_2	—	0.0394	0.0781	0.1375
F. p.	7.341°	7.115°	6.885°	6.561°
$(\theta/m_2)'$	—	6.15	6.27	6.11

(*d*) Molality of $KHSO_4 = 0.0883$

—	0.0181	0.0371	0.0762	0.1481
9.455°	9.350°	9.241°	9.031°	8.658°
—	5.92	5.89	5.70	5.54

(*e*) Molality of $KHSO_4 = 0.1528$

m_2	—	0.0170	0.0366	0.0758	0.1430
F. p.	8.668°	8.581°	8.482°	8.286°	7.944°
$(\theta/m_2)'$	—	5.30	5.28	5.24	5.29

(*f*) Molality of $NH_4HSO_4 = 0.0790$

—	0.0213	0.0401	0.0772	0.1378
9.573°	9.446°	9.543°	9.137°	8.835°
—	6.09	5.84	5.78	5.50

(*g*) Molality of acetone (as $BH^+ \cdot HSO_4^-$) $= 0.0981$

m_2	—	0.0183	0.0375	0.0714	0.1355
F. p.	9.372°	9.260°	9.145°	8.945°	8.582°
$(\theta/m_2)'$	—	6.26	6.21	6.14	6.01

(*h*) Molality of $H_2S_2O_7 = 0.130$

—	0.0217	0.0383	0.0821	0.1529
9.502°	9.378°	9.294°	9.060°	8.716°
—	5.71	5.44	5.39	5.14

(*i*) Molality of $H_2S_2O_7 = 0.313$

m_2	—	0.0486
F. p.	8.236°	8.024°
$(\theta/m_2)'$	—	4.36

(*j*) Pure acid as solvent without third component

—	0.0183	0.0356	0.0743	0.1330
10.359°	10.241°	10.140°	9.910°	9.574°
—	6.46(?)	6.17	6.07	5.95

TABLE 2. *Molecular depressions of* 1 : 3 : 5*-trinitrobenzene.*

(*a*) Molality of $(H_3O^+ \cdot HSO_4^-) = 0.089$

m_2	—	0.0428	0.0803	0.1534
F. p.	9.560°	9.290°	9.060°	8.635°
$(\theta/m_2)'$	—	6.45	6.39	6.14

(*b*) Molality of $(H_3O^+ \cdot HSO_4^-) = 0.168$

—	0.0269	0.0506	0.0993	0.1720
8.708°	8.542°	8.404°	8.162°	7.696°
—	6.41	6.26	6.24	6.17

(*c*) Molality of $KHSO_4 = 0.0746$

m_2	—	0.0866	0.1591
F. p.	9.558°	9.058°	8.898°
$(\theta/m_2)'$	—	5.91	5.80

(*d*) Molality of $KHSO_4 = 0.1524$

—	0.0200	0.0410	0.0844	0.1533
8.684°	8.581°	8.472°	8.241°	7.896°
—	5.34	5.37	5.46	5.37

(*e*) Molality of $H_2S_2O_7 = 0.116$

m_2	—	0.0239	0.0462	0.0939	0.1750
F. p.	9.612°	9.477°	9.353°	9.100°	8.679°
$(\theta/m_2)'$	—	5.64	5.61	5.45	5.33

(*f*) Pure acid as solvent without third component

—	0.0187	0.0355	0.0687	0.1179	0.1897
10.354°	10.238°	10.132°	9.925°	9.637°	9.226°
—	6.23	6.27	6.27	6.12	6.01

TABLE 3. *Molecular depressions of* 2 : 4 : 6*-trinitrotoluene.*

(*a*) Molality of $(H_3O^+ \cdot HSO_4^-) = 0.169$

m_2	—	0.0190	0.0424	0.0805	0.1425
F. p.	8.693°	8.577°	8.432°	8.195°	7.816°
$(\theta/m_2)'$	—	6.36	6.41	6.46	6.45

(*b*) Molality of $(H_3O^+ \cdot HSO_4^-) = 0.300$

—	0.0413	0.0833	0.1547
7.312°	7.059°	6.806°	6.383°
—	6.56	6.53	6.48

(*c*) Molality of $KHSO_4 = 0.0783$

m_2	—	0.0172	0.0399	0.0788	0.1350
F. p.	9.571°	9.470°	9.337°	9.112°	8.789°
$(\theta/m_2)'$	—	5.97	5.99	6.02	5.94

(*d*) Molality of $KHSO_4 = 0.1542$

—	0.0204	0.0388	0.0731	0.1381
8.660°	8.555°	8.452°	8.268°	7.910°
—	5.33	5.57	5.58	5.67

TABLE 4. *Molecular depressions of nitromethane.*

(*a*) Molality of $(H_3O^+ \cdot HSO_4^-) = 0.093$

m_2	—	0.0090	0.0466	0.0929	0.1468
F. p.	9.511°	9.453°	9.229°	8.934°	8.590°
$(\theta/m_2)'$	—	6.55	6.14(?)	6.37	6.46

(*b*) Molality of $KHSO_4 = 0.0821$

m_2	—	0.0183	0.0404	0.1210	0.1696
F. p.	9.543°	9.430°	9.288°	8.765°	8.462°
$(\theta/m_2)'$	—	6.30	6.45	6.60	6.56

(*c*) Pure acid as solvent without third component

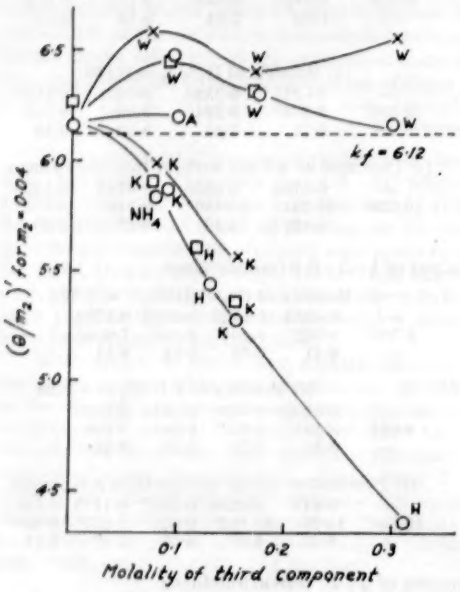
—	0.0909
10.355°	9.818°
—	6.15

fallen to 7.753°, and after 4½ hr. to 7.696° : similarly the value 6.383° (Table 3*b*) was reduced to 6.144° after 7½ hr. Thus, whatever the nature of this photochemical reaction, it is such as to cause a sufficient increase in the molecular depression to be a possible source of error in any

lengthy physical investigations involving this substance. Mr. B. J. Kirkbride has recently observed that nitromethane also undergoes some reaction in sulphuric acid since there is a slow drift of the freezing-point with time. (Dr. R. J. Gillespie informs us that he has come to the same conclusion from conductivity measurements.)

Discussion

The Tables show that the value of the overall molecular depression varies with the concentration of the nitro-compound (except trinitrotoluene usually) and with that of the third component. The two values quoted by Hammett and Deyrup for picric acid, showing deviations from K_f (6·12), fit in well with this pattern. To clarify the general trends observed, values of $(\theta/m_2)'$ have been interpolated for a 0·04*m*-concentration of the



Molecular depressions of polynitro-compounds in sulphuric acid.
○ Picric acid.
□ Trinitrobenzene.
× Trinitrotoluene.

The third components are indicated by letters as follows :
K, $KHSO_4$.
NH_4, NH_4HSO_4.
W, $H_3O{\cdot}HSO_4$.
H, $H_2S_2O_7$.
A, $(CH_3)_2C(OH){\cdot}HSO_4$.

three polynitro-compounds and plotted in the diagram against the molality of the third component : the point at 0·074*m*-water for trinitrotoluene has been taken from Gillespie's results (*loc. cit.*, p. 2544). If a higher molality of nitro-compound had been chosen the picture would have been similar, apart from some flattening of the water curve for picric acid and trinitrobenzene. Qualitatively, the three polynitro-compounds are seen to behave in the same way, although the trinitrotoluene curves are somewhat higher than the other two, giving rise to the general appearance of a sheaf of curves reminiscent of those found for activity effects in other solvents. The curves show clearly that the behaviour of these compounds is quite different in the presence of potassium and ammonium hydrogen sulphates from that in the presence of hydroxonium hydrogen sulphate, whilst acetone seems to have little effect at all. These facts eliminate the possibility of straightforward basic behaviour of the type considered by Gillespie, since such a hypothesis would require similar effects to be produced by all solutes which give rise to hydrogen sulphate ions. Other types of chemical reaction are still conceivable, but would have to be brought to terms with the spectrophotometric evidence of Brand *et al.* On the whole, it seems, however, that salting-out and salting-in effects could provide an adequate explanation, and must in any case always be considered in a three-component system (Wyatt, *J.*, 1954, 2647). Our data are neither extensive nor accurate enough for the calculation of activity coefficients by McKay's method (*Nature*, 1952, **169**, 464; McKay and Perring, *Trans. Faraday Soc.*, 1953, **49**, 163; Robinson, *ibid.*, p. 1411), although this method can be adapted for cryoscopic

determinations; but qualitatively it follows that salting-out of the non-electrolyte would be accompanied by an increase of $(\vartheta/m_2)'$, and salting-in by a decrease. Thus, if the differences of behaviour persist up to the limit of solubility, the solubilities of the polynitro-compounds should be less in slightly aqueous sulphuric acid than in dilute oleum or solutions of potassium and ammonium hydrogen sulphates; and this aspect of the problem is being investigated further. There is some evidence that non-electrolytes do in fact behave in this way; for sulphur dioxide, which has been regarded as undergoing no chemical reaction in sulphuric acid (Gold and Tye, *J.*, 1950, 2932), has been shown to have an inflection in its solubility near, but not at, 100% sulphuric acid (Miles and Carson, *J.*, 1946, 786). At 20° a minimum solubility occurs at 80·64—80·81% sulphur trioxide (*i.e.*, 98·79—99·00% sulphuric acid), after which the solubility rises steadily through 81·63% sulphur trioxide (100% sulphuric acid) and so becomes larger on the sulphur trioxide side than on the water side of 100% sulphuric acid. [A similarly displaced minimum in the density recorded by Lichty (Landolt–Börnstein's " Tabellen," Hauptwerk I, 399, footnote) does not seem to have been substantiated in the recent work of Gillispie and Wasif, *J.*, 1953, 215.]

The measurements on picric acid and trinitrobenzene at low molalities suggest that the molecular depression does not agree with Raoult's law even in the pure solvent. This is not unexpected for dilute solutions of non-electrolytes in dissociating solvents, since the solute would generally be expected to interact differently with the various species present in the pure solvent, especially where differences of polarity are possible [see *e.g.*, Rushbrooke, " Introduction to Statistical Mechanics, " O.U.P., London, 1949, p. 226, condition (*b*)].

Nitromethane differs from the polynitro-compounds in giving similar results in the presence of $KHSO_4$ and $H_3O^+ \cdot HSO_4^-$. Here, it seems, the possibility of basic behaviour cannot be ruled out, but would presumably be superimposed on salt effects in such a way that the two phenomena would be difficult to disentangle.

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SHEFFIELD UNIVERSITY. [*Received, May 12th*, 1955.]

A New Application of the Theory of Corresponding Solutions to Measurements of the Stabilities of Some Metal Complexes.

By HARRY IRVING and DEREK H. MELLOR.

[Reprint Order No. 6378.]

Solutions of identical absorption spectrum can be prepared containing the same total concentration of ferrous iron, but different proportions of 1 : 10-phenanthroline and a second cation. The theory of such " corresponding solutions," in which two metals are competing for the same ligand, is developed and applied to measurements, by two procedures, of parts of the formation curves for the systems cobalt, nickel, copper, and zinc with 1 : 10-phenanthroline. These confirm the stability constants obtained by a partition method (Irving and Mellor, to be published).

DISCORDANT values have been reported by different authors, using different procedures, for the stability constants of complexes of certain transition metals. The value $\log \beta_3 = 21{\cdot}15$ obtained for the system Fe^{2+}–1 : 10-phenanthroline by a partition method (Irving and Mellor, to be published) agrees well with the values $\log \beta_3 = 21{\cdot}5$ by a kinetic method (Lee, Kolthoff, and Leussing, *J. Amer. Chem. Soc.*, 1948, **70**, 3596), 21·3 by an equilibrium method (*idem, ibid.*, p. 2348), and 21·1 by a tracer exchange method (Cook and Long, *ibid.*, 1951, **73**, 4119). But the value 17·1 ± 0·8 has been obtained by potentiometric measurements (Dwyer and Nyholm, *J. Proc. Roy. Soc. N.S.W.*, 1946, **80**, 28) and 22·4 is reported by Davies and Dwyer (*Trans. Faraday Soc.*, 1953, **49**, 180; personal communication from Dunstone and Mellor). For the nickel–phenanthroline system the value $\log \beta_3 = 23{\cdot}9$

recently obtained by a partition method (Irving and Mellor, *loc. cit.*). disagrees with that, 18·3 ± 1·1, reported by Davies and Dwyer (*loc. cit.*); other discrepancies will be noted in a later paper (Irving and Mellor, *loc. cit.*).

An independent check on the data obtained by our partition procedure was clearly desirable. Polarographic methods are of limited value for this purpose. Thus the reduction of the trisphenanthroline complex may be irreversible, as has been demonstrated for copper (Onstott and Laitinen, *J. Amer. Chem. Soc.*, 1950, **72**, 4724) and the intrinsic difficulty of obtaining individual step-constants from polarographic measurements is now well recognised (cf. Ringbom and Eriksson, *Acta Chem. Scand.*, 1953, **7**, 1105; Eriksson, *ibid.*, p. 1146). Few reversible metal electrodes are suitable for potentiometric studies using the central-ion method (cf. Bjerrum and Nielsen, *ibid.*, 1948, **2**, 297), and any procedures based on changes in the Fe^{3+}/Fe^{2+} redox potential suffer from several disabilities: (i) phenanthroline forms complexes with both ferrous and ferric ions—although in their calculations Dwyer and Nyholm (*loc. cit.*) ignored the admittedly weaker complexing of ferric ions; (ii) the system comes to equilibrium rather slowly; (iii) the organic component may be irreversibly oxidised. We have, however, succeeded in confirming the values we had previously reported for the stability constants of several transition-metal–phenanthroline complexes by a novel application of the theory of corresponding solutions which is capable of still wider use.

When a series of metal complexes MA_n ($n = 1, 2, \ldots N$) formed from a metal, M, and a ligand, A, are in a stepwise equilibrium governed by stability constants defined by $K_n = [MA_n]/[MA_{n-1}][A]$, or $\beta_n = [MA_n]/[M][A]^n$, it is well known that the ligand number, $\bar{n}$, is a function only of [A], the concentration of free ligand (*i.e.*, that which is not bound in any way, *e.g.*, to metal or to hydrogen ions), and the various stability constants $\beta_1, \beta_2, \ldots \beta_N$.

Explicitly
$$\bar{n} = \sum_0^N n\beta_n[A]^n \Big/ \sum_0^N \beta_n[A]^n \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where $\beta_0 = 1$, by definition. The fraction of the total metal present in the form MA_n is given by

$$\alpha_n = \beta_n[A]^n \Big/ \sum_0^N \beta_n[A]^n \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

and the ratio between the concentrations of any two species MA_n and MA_j by

$$r_{n,j} = [MA_n]/[MA_j] = \beta_n[A]^{n-j}/\beta_j \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

Since α_n and $r_{n,j}$ are functions only of [A] and the stability constants $\beta_1, \beta_2, \ldots \beta_N$, they are also functions of $\bar{n}$; but they do not contain terms specifically relating to the total concentrations of metal or ligand in the system. Now if C_M is the total concentration of metal present, and C_A the total concentration of ligand available for complex formation with it (*i.e.*, excluding the amount bound to protons or to any other metal present), we have

$$\bar{n}_M = (C_A - [A])/C_M$$

or
$$C_A = \bar{n}_M \, . \, C_M + [A] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

Any increase in the total concentration of metal from C_M to C_M' (or C_M'', . . .) will produce a decrease in $\bar{n}_M$ which can be exactly compensated by an increase in the total concentration of ligand from C_A to C_A' (or C_A'' . . .), so that

$$\bar{n}_M = (C_A - [A])/C_M = (C_A' - [A])/C_M' = (C_A'' - [A])/C_M'' = \ldots\ldots$$

$\bar{n}$ and [A] remaining the same in all cases. Clearly an infinite number of solutions could be prepared for which the values of C_A and C_M satisfy the linear equation (4) where $\bar{n}$ and [A] are now constants. Such solutions are said to be "corresponding" (Bjerrum, *Kgl. Dansk Videnskab. Selskab.*, 1944, **21**, No. 4; Fronaeus, *Acta Chem. Scand.*, 1951, **5**, 139) and it follows from (2) and (3) that α_n (and $r_{n,j}$) is the same for all of them. Conversely, any physical property which permits the quantitative measurement of α_n (or $r_{n,j}$) may

serve to establish the " correspondence " between solutions, and equation (4) can then be solved for $\bar{n}$ and [A]. The determination of the values of the constants β_1, β_2, . . . β_N from pairs of values of $\bar{n}$ and [A] has been discussed previously (Irving and Rossotti, *J.*, 1953, 3397).

FIG. 1. *The absorbancy, A_s, at 510 mμ, of solutions containing 8 × 10⁻⁵M-ferrous iron and increasing concentrations of 1 : 10-phenanthroline. The concentration of cobalt, C_M, in curves 1, 2, 3, 4, and 5 was 0, 1·2, 1·6, 2·4, and 3·2 × 10⁻⁴M.*

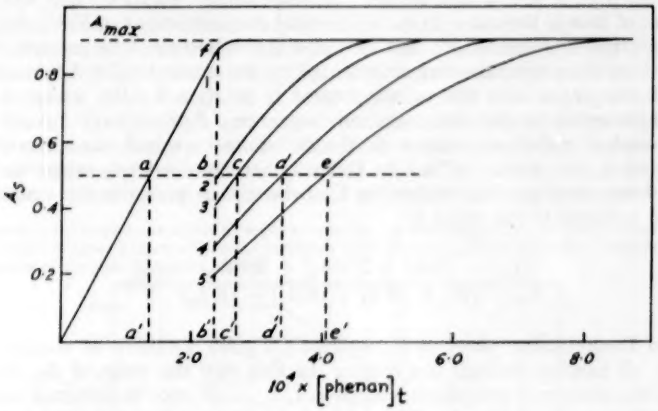
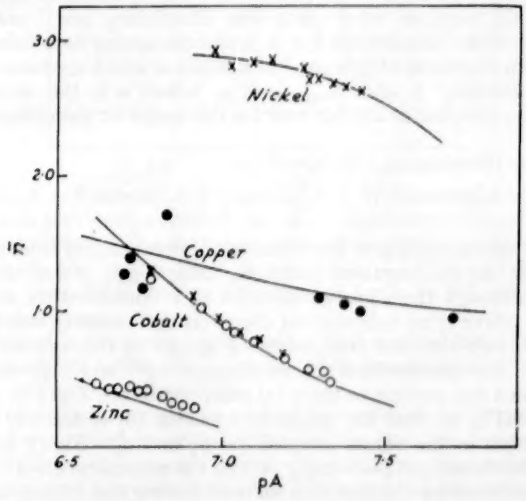


FIG. 2. *The results of spectrophotometric determination of the stability constants of metal–phenanthroline complexes. The full lines are formation curves drawn by using stability constants obtained previously by a partition method.*



The method of applying the theory of corresponding solutions to the present problem is illustrated by Fig. 1. Curve 1 shows the effect of increasing total concentrations of 1 : 10-phenanthroline, $[phenan]_t$, on the absorbancy at 510 mμ of a solution 8 × 10⁻⁵M with respect to ferrous iron and of a constant ionic strength 0·1M. Curve 2 was obtained by making similar measurements on solutions containing 1·2 × 10⁻⁴M-cobaltous ion in addition to the previous concentration of ferrous iron, the temperature and ionic strength remaining

the same. Curves **3**, **4**, and **5** refer to measurements in which the concentration of cobalt was increased progressively to **1·6**, **2·4**, and **3·2** $\times$ 10^{-4}M respectively. The absorbancy at 510 mμ is due essentially to the red tris-complex $Fe(phenan)_3^{2+}$. The reduction in absorbancy as the cobalt concentration is increased while the total concentration of phenanthroline remains constant (ordinate *fbb'*) is due to the smaller concentration of phenanthroline available for forming complexes with iron consequent upon the formation of the species $Co(phenan)^{2+}$, $Co(phenan)_2^{2+}$, and $Co(phenan)_3^{2+}$. Mixtures having the same absorbancy, A_s (*e.g.*, *a*, *b*, *c*, *d*, and *e*), are " corresponding " solutions and, since the total concentration of iron is the same in each, identical concentrations of Fe^{2+}, $Fe(phenan)^{2+}$, $Fe(phenan)_2^{2+}$, and $Fe(phenan)_3^{2+}$, and free phenanthroline must be present. It follows that the whole of the phenanthroline represented by the concentration difference *a'b'* must have formed complexes with the cobalt present in solution **2**; the whole of the phenanthroline represented by the concentration difference *c'd'* must have formed complexes with an amount of cobalt equivalent to the difference in cobalt concentration between solutions **3** and **4**, *viz.*, **0·8** $\times$ 10^{-4}M. In this way are obtained ten values for C_N (where N = Co) and ten corresponding values for C_A (where A = phenan), the concentration of ligand bound uniquely to the metal N.

Then
$$\frac{C_A}{C_N} = \frac{[NA] + 2[NA_2] + 3[NA_3]}{[N] + [NA] + [NA_2] + [NA_3]} = \bar{n}_N \quad . \quad . \quad . \quad . \quad (5)$$

As predicted theoretically, plots of C_A against C_N gave a family of straight lines (not reproduced), all passing through the origin. In this way the value of $\bar{n}_N$, the degree of formation of the system of complexes NA_n ($n = 1, 2, \ldots N$) can be obtained corresponding to each absorbancy, A_s, in Fig. 1. The method of corresponding solutions has previously been applied to the study of complexes of a single metal such that values of $\bar{n}$ and [A] are obtained from the same measurements as shown in equation (4). When two metals are competing for the same ligand, as in the present procedure, values of [A] must be obtained indirectly. Since all solutions of a particular absorbancy are " corresponding," the constant value of [phenan] in solutions *b*, *c*, *d*, and *e* containing both cobaltous and ferrous ions is identical with the value of [phenan] in solution *a* which contains only ferrous iron. Since $A_s = \varepsilon l[Fe(phenan)_3^{++}]$, and $A_{max.} = \varepsilon l C_{Fe}$, where ε is the molecular extinction coefficient of the tris-complex at 510 mμ and l is the length of the optical cell,

$$A_s/A_{max.} = [Fe(phenan)_3^{++}]/C_{Fe}$$
$$= \beta_3[phenan]^3/(1 + \beta_1[phenan] + \beta_2[phenan]^2 + \beta_3[phenan]^3) \quad . \quad (6)$$

Values of [phenan] corresponding to any value of A_s were read off from a large-scale graph (not reproduced) of $A_s/A_{max.}$ against [phenan], using $\log \beta_1 = 5{\cdot}85$, $\log \beta_2 = 11{\cdot}15$, and $\log \beta_3 = 21{\cdot}15$. Although the value adopted for β_3 is confirmed by several independent methods (p. 3457), there is no independent check on the values chosen for β_1 and β_2; but it can readily be shown that the predominating species in this system are the ions Fe^{2+} and $Fe(phenan)_3^{2+}$, the intermediate species $Fe(phenan)^{2+}$ and $Fe(phenan)_2^{2+}$ never contributing more than a few percent to the total composition (cf. Fig. 3 in Irving, Cabell, and Mellor, *J.*, 1953, **3417**), so that the graph of equation (6) is scarcely modified even by considerable variation in the values adopted for β_1 and β_2. Fig. 2 (crosses) shows how closely the values for $\bar{n}_N$ and pA (= $-\log_{10}$ [A]) for the system cobalt–1 : 10-phenanthroline agree with those obtained by the partition method (Irving and Mellor, *loc. cit.*) which were used to plot the formation curves shown as solid lines.

The unusual features of the system ferrous ions–1 : 10-phenanthroline already mentioned, and the fact that $K_3 \gg K_1 > K_2$, permit a further simplification in experimental procedure. Let A_0 be the absorbancy and $[phenan]_0$ the concentration of free ligand for a solution containing ferrous iron at a concentration, C_{Fe}, and phenanthroline at a concentration, C_A, somewhat less than $3C_{Fe}$; let A_1 be the absorbancy and $[phenan]_1$ the concentration of free ligand after addition of another metal N, at a concentration C_N, and

let $A_{max.}$ be the absorbancy of the first solution after the addition of excess of phenanthroline. Since $A_{max.} = dC_{Fe}$ as before, we have for the first solution

$$C_A = 3(A_0 C_{Fe}/A_{max.}) + [\text{phenan}]_0$$

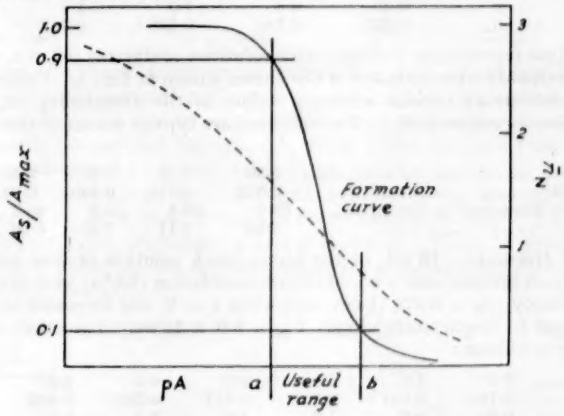
and for the second solution

$$C_A = 3(A_1 C_{Fe}/A_{max.}) + [\text{phenan}]_1 + \bar{n}_N C_N$$

whence $$\bar{n}_N = \{[\text{phenan}]_0 - [\text{phenan}]_1 + 3C_{Fe}(A_0 - A_1)/A_{max.}\}/C_N \quad . \quad . \quad . \quad (7)$$

Under the experimental conditions employed, the change in free-ligand concentration is negligible in comparison with the last term in the numerator of equation (7), which simplifies to $\bar{n}_N = 3C_{Fe}(A_0 - A_1)/A_{max.}C_N$. The corresponding value of [phenan] is obtained, as before, from the graph of equation (6). The results for cobalt are shown (open circles) in Fig. 2. The agreement with the more rigorous spectrophotometric procedure is quite satisfactory, and by using the simpler procedure values for $\bar{n}_N$ and corresponding values of pA were obtained for N = nickel, copper, and zinc, and A = 1 : 10-phenanthroline. These results are shown in Fig. 2 where the full lines were drawn with

FIG. 3. *Schematic representation of the formation curve for an arbitrary metal–1 : 10-phenanthroline system superimposed on a graph representing the variation in the fraction of trisphenanthrolineferrous ion present as a function of the free ligand exponent.*



the stability constants previously reported (*loc. cit.*). Agreement is excellent for complexes of nickel, cobalt, and copper. The data now obtained for zinc lie just above the formation curve calculated with the values $\log \beta_1 = 6{\cdot}4$, $\log \beta_2 = 11{\cdot}95$, and $\log \beta_3 = 17{\cdot}05$. A slightly better fit is given by increasing the value of $\log \beta_1$ to 6·5, without changing the values for the other two constants.

It has been assumed in the foregoing treatment that none of the optical absorbancy at 510 mμ is due to the second cation N^{2+}, or to any of its complexes NA^{2+}, NA_2^{2+}, or NA_3^{3+}. This was, of course, verified experimentally.

Although the new procedures could be applied to studies of complexes of various metals with, *e.g.*, dipyridyl—provided accurate values for the stability constants of its ferrous complexes were available—and many obvious extensions can be envisaged, they cannot provide data for plotting a complete formation curve for the competing metal, N. The reasons for this appear in Fig. 3 which represents schematically the plot of $A_s/A_{max.}$ as a function of pA (solid line) for the system ferrous iron–1 : 10-phenanthroline. The accuracy with which measurements of the ratio $A_s/A_{max.}$ can be made falls off as $A_s \longrightarrow 0$, and as $A_s \longrightarrow A_{max.}$, so that, if only values within the range $0{\cdot}1 \geqslant A_s/A_{max.} \geqslant 0{\cdot}9$ are acceptable, only those "corresponding" solutions can be studied for which the free ligand concentration lies within the range $a \geqslant \text{pA} \geqslant b$. The portion of the formation curve (broken lines) accessible to study is therefore limited as shown in Fig. 3. But, depending on the

magnitude of the stability constants of the complexes formed by the competing metal, N, the useful range will cover different portions of the respective formation curves, as shown in Fig. 2.

Experimental

Absorbancies were measured with a Unicam Spectrophotometer, model S.P. 500, with matched Corex cells in a cell compartment at 25° ± 0·1° (thermostat). Recrystallised "AnalaR" reagents were employed and the cobalt salt was tested for the absence of nickel and iron.

System, Cobaltous Ions–1 : 10-Phenanthroline.—(a) *Full procedure.* A stock solution of iron and phenanthroline was made up to contain ferrous iron (2×10^{-4}M), 1 : 10-phenanthroline ($5{\cdot}94 \times 10^{-4}$M), hydrochloric acid (0·01M), potassium chloride (0·22M), and hydroxylamine hydrochloride (0·5%). To 10 ml. portions were added x ml. of a cobaltous solution (0·01M), y ml. of 0·10% aqueous 1 : 10-phenanthroline monohydrate, and 5 ml. of 0·1M-sodium acetate, and the total volume was made up to 25 ml. at 25°. The following absorbancies, A_s, were obtained at 510 mμ with 1-cm. cells.

$x = 0{\cdot}3$	y	0·0	0·4	0·8	1·2	1·6
	A_s	0·494	0·700	0·842	0·898	0·905
$x = 0{\cdot}4$	y	0·0	0·5	1·0	1·5	2·0
	A_s	0·42	0·568	0·825	0·900	0·950
$x = 0{\cdot}6$	y	0·0	0·4	0·8	1·5	2·5
	A_s	0·290	0·464	0·616	0·818	0·898
$x = 0{\cdot}8$	y	0·00	0·5	1·0	1·5	3·0
	A_s	0·203	0·382	0·558	0·702	0·903

Additional data (not reproduced) obtained with solutions containing 0·3, 0·5, 0·7, and 0·9 ml. of 0·01M-cobaltous sulphate were included in the curves shown in Fig. 1. Values of C_A and C_N for corresponding solutions at various arbitrary values of the absorbancy, A_s, were plotted as abscissæ and ordinates respectively. The following are typical values of the calculated degrees of formation :

Absorbancy, A_s	0·30	0·42	0·50	0·60	0·70	0·80
Slope of graph, $\bar{n}$	0·672	0·775	0·840	0·945	1·10	1·29
Percentage of the tris-complex, $100A_s/A_{max.}$	33·2	46·4	55·2	66·3	77·3	88·4
$-\log_{10}$ [phenan]	7·19	7·11	7·055	6·99	6·91	6·78

(b) *Shortened procedure.* 10 ml. of the above stock solution of iron and phenanthroline, 5 ml. of 0·1M-sodium acetate, and x ml. of cobaltous solution (10^{-3}M) were made up to 25 ml. at 25°. The absorbancy, $A_0 = 0{\cdot}875$ (1-cm. cell) when $x = 0$, was increased to $A_{max.} = 0{\cdot}885$ by adding an excess of 1 : 10-phenanthroline. $C_{Fe} = 8{\cdot}0 \times 10^{-6}$M. The other measurements and calculations were as follows :

x (ml.)	0·5	1·5	3·0	4·0	6·0	8·0	9·0	1·1 *
A_1	0·785	0·651	0·500	0·417	0·283	0·196	0·160	0·104
$10^4 C_N$	0·2	0·6	1·2	1·6	2·4	3·2	3·6	4·4
$\bar{n}_N$	1·22	1·01	0·84	0·78	0·67	0·575	0·54	0·47
$-\log_{10}$ [phenan]	6·78	6·94	7·04	7·10	7·19	7·27	7·31	7·33

* A 10^{-3}M-solution of cobaltous sulphate was used for this experiment.

For measurements with other metals 10^{-3}M-solutions of nickel, zinc, or cupric sulphate were used in place of the cobaltous sulphate; hydroxylamine hydrochloride was omitted in measurements of the copper–phenanthroline system. The following is a summary of the results :

Nichel (x was varied from 0·1 to 2·0 ml.; A_s from 0·80 to 0·09) :

pA	6·97	7·02	7·09	7·14	7·24	7·26	7·29	7·33	7·37	7·42
$\bar{n}$	2·89	2·78	2·83	2·84	2·78	2·71	2·70	2·68	2·65	2·61

Zinc (x was varied from 0·3 to 5·0 ml.; A_s from 0·87 to 0·68) :

pA	6·92	6·89	6·86	6·82	6·77	6·75	6·72	6·68	6·66	6·62
$\bar{n}$	0·28	0·295	0·315	0·365	0·416	0·395	0·42	0·395	0·40	0·45

Copper (x was varied from 0·10 to 6·0 ml.; A_s from 0·81 to 0·015) :

pA	6·70	6·72	6·76	6·83	7·29	7·37	7·42	7·70
$\bar{n}$	1·25	1·37	1·18	1·70	1·09	1·06	0·98	0·93

We express our indebtedness to Messrs. Imperial Chemical Industries Limited for the gift of chemicals, and to Messrs. British Celanese Ltd. for the award of a Senior Studentship to one of us (D. H. M.).

The Inorganic Chemistry Laboratory, Oxford. [*Received, May 2nd,* 1955.]

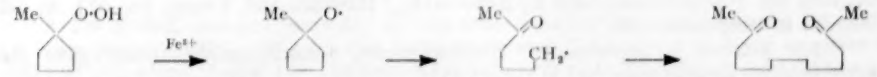
Reactions of Organic Peroxides. Part VII. Reaction of 1-Hydroxycycloalkyl Hydroperoxides with Ferrous Compounds.*

By E. G. E. Hawkins.

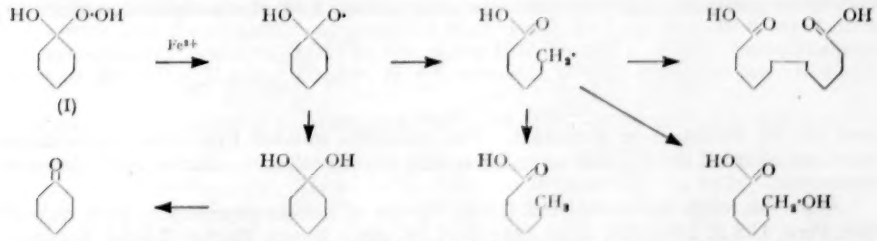
[Reprint Order No. 6408.]

The liquid peroxide first formed on addition of hydrogen peroxide to *cyclo*hexanone reacted with ferrous sulphate solution to yield dodecane-1 : 12-dioic and hexanoic acid; solid peroxides gave much lower yields of the dicarboxylic acid. Peroxides derived from other *cyclo*alkanones gave less of the corresponding dicarboxylic acids. Autoxidation of *cyclo*hexyl ethers gave poor yields of the 1-hydroperoxides, which, with ferrous sulphate, provided esters of dodecane-1 : 12-dioic acid.

During the study of the decomposition of tertiary *cyclo*alkyl hydroperoxides it was found that a diketone was produced in small yield by thermal treatment (Gasson, Hawkins, Millidge, and Quin, *J.*, 1950, 2798; Hawkins, *J.*, 1950, 2801), but in higher yield by reaction with ferrous sulphate solution (Hawkins and Young, *J.*, 1950, 2804). *E.g.*:



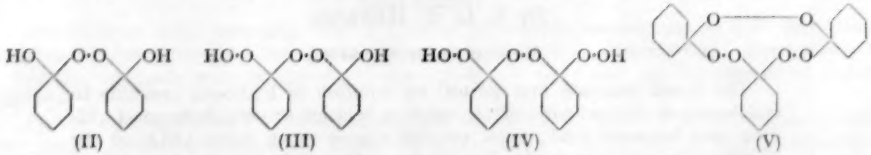
The corresponding dibasic acids, given only in low yield by thermal decomposition of 1-hydroxy*cyclo*alkyl hydroperoxides (Cooper, *J.*, 1951, 1340), were similarly produced in improved yield (*ca.* 50%) by ferrous sulphate treatment of the peroxide. After this work had been completed, Cooper and Davison (*J.*, 1952, 1180) reported that ferrous sulphate reaction led to dodecane-1 : 12-dioic acid (from *cyclo*hexanone) in unspecified yield. Other products of this reaction, hexanoic acid, *cyclo*hexanone, and possibly 6-hydroxyhexanoic acid, could all have been derived from a common radical, although part of the *cyclo*hexanone was probably unchanged starting material. These by-products were of the same type as those obtained on decomposition of 1-methyl*cyclo*pentyl hydroperoxide (Hawkins and Young, *loc. cit.*).



The peroxides were obtained by addition of hydrogen peroxide to *cyclo*alkanones. The peroxides formed under these conditions are ill-defined, and several different compounds derived from *cyclo*hexanone have been reported (Milas, Harris, and Panagiotakos, *J. Amer. Chem. Soc.*, 1939, **61**, 2430; Criegee, Schnorrenberg, and Becke, *Annalen*, 1949, **565**, 7); the reaction of some of these compounds with ferrous sulphate provided evidence on this problem. When *cyclo*hexanone was mixed with 90% hydrogen peroxide a slightly exothermic reaction led to a syrup which reacted smoothly with ferrous sulphate solution to give up to 55% of dodecane-1 : 12-dioic acid. This syrup gradually crystallised, and crystalline peroxides were also obtained from *cyclo*hexanone and 30% or 5% hydrogen peroxide, with or without hydrochloric acid as catalyst. Such solid peroxides gave poor yields of the dicarboxylic acid when treated with ferrous sulphate solution, suggesting that the liquid peroxide was mainly (I), whilst the solid peroxides were of the type (II)—(V)

* Part VI, *J.*, 1953, 4106.

which would be expected to react with ferrous ion with greater difficulty owing to the greater stability of the –O·O– linkage than that of the –O·OH group. The presence of residual peroxide at the end of the reaction confirmed this increased stability.



(II) (III) (IV) (V)

The peroxide obtained by uncatalysed reaction of *cyclo*hexanone with 5% hydrogen peroxide gave analyses correct for (II), but its m. p. (91—93°) was nearer that reported by Criegee *et al.* (*loc. cit.*) for the trimer (V) (m. p. 93°) than for the dimer (II) (m. p. 68—70°). The peroxide formed in the presence of hydrochloric acid had an analysis and m. p. (80·5—81·5°) close to that reported for the compound (IV) (m. p. 83°); this compound was decomposed by ferrous sulphate more readily than that obtained from the uncatalysed reaction.

Replacement of ferrous sulphate by ferrous chloride led to very low conversion into the C_{12} acid (cf. 1-methyl*cyclo*pentyl hydroperoxide; Hawkins and Young, *loc. cit.*), as did increase in temperature (50°).

Other ketones (*cyclo*pentanone, *cyclo*heptanone, 4-methyl*cyclo*hexanone) gave the corresponding dibasic acids, but in lower yields.

Direct preparation of esters of these dicarboxylic acids depended on the initial formation of 1-alkoxy*cyclo*alkyl hydroperoxides. Formation of such compounds by autoxidation of *cyclo*hexyl ethers proved troublesome, and similar difficulties were encountered as during the oxidation of methyl*cyclo*pentane and methyl*cyclo*hexane (Gasson *et al.*, *loc. cit.*), *i.e.*, the peroxide concentration rose to *ca.* 10% and then fell rapidly owing to decomposition. Autoxidation of *cyclo*hexyl methyl ether yielded some peroxide, difficult to isolate, together with *cyclo*hexanone and adipic acid; di*cyclo*hexyl formal also gave traces of peroxide, as well as *cyclo*hexanol, *cyclo*hexanone, formic and adipic acid, and *cyclo*hexyl esters of these acids. Autoxidation of the *cyclo*hexyl ketal of acetone (2 : 2-di*cyclo*hexyloxypropane) yielded *cyclo*hexanol, *cyclo*hexanone, and *cyclo*hexyl formate, acetate, and adipate, but very little peroxide. All these products were derived from the mesomeric radicals (*A*)

(*A*) (*B*)

and (*B*) by oxidation or reduction. The peroxides isolated from these autoxidation reactions afforded the C_{12} acid on reaction with ferrous sulphate solution and subsequent hydrolysis.

After this work was completed (1951), details of similar experiments were reported (Du Pont, U.S.P. 2,601,223, 2,601,224; B.P. 697,506; Brown, Hartig, Roedel, Anderson, and Schweitzer, *J. Amer. Chem. Soc.*, 1955, **77**, 1756).

Experimental

cyclo*Hexanone.*—(a) *Use of concentrated hydrogen peroxide.* *cyclo*Hexanone (50 c.c.) and hydrogen peroxide (90%; 20 g.) were mixed, with cooling, and used, sometimes within ½ hr., and sometimes after being kept overnight, before crystallisation set in. The liquid mixture was added, during ½—1 hr., with stirring, to a suspension of powdered ferrous sulphate (250 g.) in water or 2N-sulphuric acid (500 c.c.), at temperatures which were varied from 0° to 50°. The product was extracted with ether, and the solvent evaporated; the residue was poured into light petroleum (b. p. 40—60°) and the solid dodecane-1 : 2-dioic acid (23·0 g.) filtered off. This acid had m. p. 125—126·5° (from benzene) (Found: C, 62·1; H, 9·5%; equiv., 116·5. Calc. for $C_{12}H_{22}O_4$: C, 62·6; H, 9·6%; equiv., 115). The filtrate was freed from petroleum and provided a distillate (18·0 g.), b. p. 60—150°/15 mm., and a residue (5·5 g.) from which further C_{12} acid (0·8 g.) was isolated. The distillate was separated into neutral and acid products by treatment

with alkali. The neutral product was mainly *cyclo*hexanone (9·2 g.) (2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 161—162°), and the acids (8·7 g.) were separated by distillation into hexanoic acid (*p*-bromophenacyl ester, m. p. and mixed m. p. 68—70°) and a high-boiling (?) hydroxy-acid. The effect of varying the temperature and reagent in further experiments is shown in Table 1.

TABLE 1.

Fe salt (g.)	Solvent (c.c.)	Temp.	Time of addition (min.)	Products (g.) C_{12} Acid	*cyclo*-Hexanone	C_6 Acids	Residue
$FeSO_4,7H_2O$							
260	H_2O (500)	Room	45 *	22·6	9·0	7·3	5·7
260	2N-H_2SO_4 (500)	,,	5 *	15·5	13·2	5·7	2·5
350	2N-H_2SO_4 (500)	,,	45 *	19·0	11·6	6·0	3·6
250	2N-H_2SO_4 (500)	50°	30 *	6·9	15·8	4·1	2·5
250	H_2O (500)	0—5	45 *	23·8	6·3	9·8	4·7
250	2N-H_2SO_4 (500)	0—5	45 †	25·8	7·7	5·8	2·5
125	2N-H_2SO_4 (250)	0—5	45 ‡	>8·5	17·5	7·7	5·4
$FeCl_2,4H_2O$							
200	H_2O (500)	Room	45 *	0·5	11·7	34·2	1·0

* Peroxide from *cyclo*hexanone (50 c.c.) and 90% H_2O_2 (* 20 g., † 25 g., ‡ 10·5 g.).

(b) *Use of* 30% *hydrogen peroxide.* (i) The solid peroxide from *cyclo*hexanone (50 c.c.), hydrogen peroxide (30%; 50 c.c.), and hydrochloric acid (2 c.c.), was dissolved in ethanol (100 c.c.) and added (during 1 hr.) to ferrous sulphate (250 g.) in 2N-sulphuric acid (500 c.c.). The product was separated into C_{12} acid (5·1 g.), *cyclo*hexanone (17·9 g.), hexanoic acid (7·6 g.), and residue (11·8 g.).

(ii) A mixture of *cyclo*hexanone and hydrogen peroxide as in (i) but excluding hydrochloric acid, added to acidified ferrous sulphate solution within 1 hr., yielded C_{12} acid (16·8 g.), *cyclo*hexanone (13·8 g.), hexanoic acid (6·9 g.), and residue (4·3 g.).

(c) *Use of* 5% *hydrogen peroxide.* Addition of *cyclo*hexanone (25 g.) to 5—6% hydrogen peroxide (200 c.c.) gave, on storage, a solid peroxide (A) (25—26 g.) similar to that which separated gradually from the mixture of 90% hydrogen peroxide and ketone. This peroxide had m. p. 91—93° (from benzene) [Found: C, 60·2; H, 9·7; active H (Zerewitinov), 0·64, 0·94%; peroxide equiv., 221—239. Calc. for $(HO{\cdot}C_6H_{10}{\cdot}O)_2$: C, 62·6; H, 9·6; active H, 0·87%; peroxide equiv., 230].

Addition of *cyclo*hexanone (25 g.) to 6% hydrogen peroxide (200 c.c.) containing concentrated hydrochloric acid (5 c.c.) yielded, on storage, a peroxide (B) (25·7 g.), m. p. 80·5—81·5° (from aqueous methanol) [Found: C, 55·3; H, 7·9; active H (Zerewitinov), 0·75%; peroxide equiv., 88. Calc. for $(HO_2{\cdot}C_6H_{10}{\cdot}O)_2$: C, 55·0; H, 8·4; active H, 0·76%; peroxide equiv., 87·3].

TABLE 2. *Treatment of peroxides with* $FeSO_4,7H_2O$ (125 *g.*) *in* 2N-H_2SO_4 (250 *c.c.*).

Peroxide used	Temp.	Products (g.) C_{12} Acid	*cyclo*Hexanone	C_6 Acids	Residue
A; 25 g.	0—5°	2·6	3·8	3·6	1·3
A; 25 g. in EtOH (90 c.c.)	,,	4·4	6·8	2·5	2·5
A; 25 g. in acetone (170 c.c.)	,,	3·9	5·5	2·0	2·6
					Peroxide *
B; 25 g.	,,	1·3	7·3	6·0	6·6
B; 25 g. in EtOH (60 c.c.)	,,	1·6	5·5	5·5	1·7
B; 25 g. in acetone (88 c.c.)	,,	1·0	7·5	7·5	1·0
					Residue
C †	Room	8·0	11·5	7·6	12·3

* The products from experiments with peroxide B could not be distilled owing to the presence of undecomposed peroxide; the quantites of *cyclo*hexanone, C_6 acids, and peroxides in the residue were obtained by analysis. Peroxides A and B are described above. † A mixture of *cyclo*hexanone (50 c.c.) and hydrogen peroxide (5%; 350 c.c.) added to the ferrous sulphate solution (250 g. of $FeSO_4,7H_2O$ in 500 c.c. of 2N-H_2SO_4) before crystallisation had set in.

The results of treatment of these solid peroxides, as well as of an uncrystallised mixture of ketone and 5% hydrogen peroxide, with ferrous sulphate solution, are given in Table 2.

Other Ketones.—(i) cyclo*Pentanone.* The ketone (50 g.) was mixed with 90% hydrogen peroxide (23 g.), kept for 2 hr., and added to ferrous sulphate (250 g.) in 2N-sulphuric acid

(500 c.c.). Working up gave sebacic acid (5·5 g.) (m. p. and mixed m. p. 130—131·5°), *cyclo*pentanone (18·1 g.), valeric acid (2·0 g.) (*p*-bromophenacyl ester, m. p. and mixed m. p. 73—74°), and residue (5·6 g.).

(ii) cyclo*Heptanone*. The ketone (25 g.), 30% hydrogen peroxide (30 g.), and concentrated hydrochloric acid (1 c.c.) were set aside for 3 days and then added to ferrous sulphate (125 g.) in 2N-sulphuric acid (250 c.c.). Ether-extraction of the product followed by distillation gave *cyclo*heptanone (8·5 g.), *n*-heptanoic acid (*p*-bromophenacyl ester, m. p. 68·5—70°), and tetradecane-1 : 14-dioic acid (3·5 g.), m. p. 122—123·5° (from benzene–light petroleum) (Found: C, 65·2; H, 9·5%; equiv., 128·3. Calc. for $C_{14}H_{26}O_4$: C, 65·1; H, 10·1%; equiv., 129).

(iii) 4-*Methyl*cyclo*hexanone*. After the ketone (50 g.) had been kept overnight in 90% hydrogen peroxide (20 g.), the mixture was gradually added to stirred ferrous sulphate (250 g.) in 2N-sulphuric acid (500 c.c.). The product, on distillation, provided fractions containing 4-methyl*cyclo*hexanone (12·5 g.), 4-methylhexanoic acid (*ca.* 10 g.), b. p. 208—212° [amide, m. p. 95—96° (Found: C, 64·6; H, 11·4; N, 11·1. Calc. for $C_7H_{15}ON$: C, 65·1; H, 11·6; N, 10·8%); anilide, m. p. 75—76·5° (Found: C, 75·4; H, 9·1; N, 7·2. Calc. for $C_{13}H_{19}ON$: C, 76·1; H, 9·3; N, 6·8%); p-*bromophenacyl* ester, m. p. 45—46° (Found: C, 55·0; H, 5·75; Br, 24·7. $C_{15}H_{19}O_3Br$ requires C, 55·0; H, 5·8; Br, 24·5%)], and high-boiling material (21 g.) from which 4 : 9-*dimethyldodecane*-1 : 12-*dioic acid*, m. p. 94—95·5° (from benzene–light petroleum) (Found: C, 65·3; H, 9·8%; equiv., 131. $C_{14}H_{26}O_4$ requires C, 65·1; H, 10·1%; equiv., 129), was isolated.

(iv) 2-Methyl*cyclo*hexanone and α-tetralone did not yield dicarboxylic acids under the conditions used.

Oxidation of cyclo*Hexyl Ethers*.—(a) cyclo*Hexyl methyl ether*. This ether was prepared in yields of *ca.* 50% by gradual addition of methyl sulphate (256 g.) to sodium *cyclo*hexyloxide [from reaction of sodium (46 g.) with heated and stirred *cyclo*hexanol (200 g.) in di*iso*propylbenzene (256 g.)] or *ca.* 40% by addition of methyl sulphate (250 g.) to a solution of sodamide (78 g.) and *cyclo*hexanol (200 g.) in diethyl ether (1500 c.c.). The crude, distilled products were refluxed over sodium and redistilled, then having b. p. 132—133°; n_D^{20} 1·4355 (lit., b. p. 135—136°, n_D^{20} 1·4344).

On oxidation at 100—110°, with or without catalyst and inorganic bases, the maximum peroxide concentration was *ca.* 14%; continued oxidation led to decomposition of peroxide and formation of *cyclo*hexanone and adipic acid.

(i) The ether (50 g.), treated with oxygen at 110°, without catalyst, contained 10% of peroxide after 6 hr. Acid products were removed with sodium carbonate solution, and unchanged ether (29 g.) removed from the neutral residue at the water-pump. The product gave a distillate (1·2 g.), b. p. 55—60°/0·2 mm. (Found: peroxide equiv., 186·4. Calc. for 1-Methoxy-*cyclo*hexyl hydroperoxide: peroxide equiv., 146), and a residue containing esters from which adipic acid, m. p. 149—150° [Found: equiv., 75. Calc. for $C_4H_8(CO_2H)_2$: equiv., 73] (*p*-bromophenacyl ester, m. p. and mixed m. p. 154—156°), was obtained on hydrolysis. The distillate, on treatment with acidified ferrous sulphate solution, followed by hydrolysis, yielded dodecane-1 : 12-dioic acid (recrystallised; 0·3 g.), m. p. 125·5—126·5°.

(ii) The ether (100 g.) was oxidised at 100° for 20 hr., the peroxide concentration reaching 14%. Unchanged ether was removed and the crude residue (19·5 g.; 43·5% of peroxide) added to ferrous sulphate solution. There was finally obtained *cyclo*hexanone, hexanoic acid (1·2 g.), C_{12} acid (1·4 g.), and residue (1·3 g.).

(b) cyclo*Hexyl formal*. This was prepared by a modification of Sabetay and Schving's method (*Bull. Soc. chim. France*, 1928, **43**, 1342), and had b. p. 140°/15 mm., $n_D^{19\cdot5}$ 1·4705. Much decomposition occurred during oxidation at 100—110°, the peroxide concentration did not exceed 10%, and from the products were isolated formaldehyde, formic acid, *cyclo*hexanone, *cyclo*hexyl formate and adipate, and free adipic acid. Concentration of the peroxide by distillation or alkali-extraction proved difficult owing to its ease of decomposition. In one experiment, oxidation of the formal (50 g.) for 3¼ hr. at 110° was followed by dilution with light petroleum and washing with cold 50% sodium hydroxide solution (10 c.c.) to remove the peroxide. The extract was washed with benzene and light petroleum, suspended in cold water, treated with carbon dioxide, and extracted with diethyl ether. Evaporation of the ether left a residue (1·0 g.; *ca.* 50% of peroxide), which after reaction with ferrous sulphate and hydrolysis yielded a small quantity of dodecane-1 : 12-dioic acid, m. p. 122—124°.

This acid was also isolated from the products obtained by treatment of a crude oxidate with ferrous sulphate.

(c) 2 : 2-*Di*cyclo*hexyloxypropane*. Ethyl orthoformate (100 g.), *cyclo*hexanol (300 c.c.), and

concentrated hydrochloric acid (few drops) were heated and distilled through a short column. When the calculated quantity of ethanol had been removed, the product was distilled to give *cyclo*hexanol and cyclo*hexyl orthoformate* (81·0 g.; b. p. 200—205°/15 mm.), m. p. 72—73° (from benzene–light petroleum) (Found: C, 72·8; H, 11·0. $C_{19}H_{34}O_3$ requires C, 73·5; H, 11·0%). Ethyl orthoformate (100 g.), *cyclo*hexanol (300 g.), and concentrated hydrochloric acid (few drops) were added to acetone (60 g.) and concentrated sulphuric acid (one drop) and set aside for 1 hr.; the product was washed with ammonia and water, dried, and distilled to provide the *ketal* (64 g.), b. p. *ca.* 140°/15 mm. (Found: CO equiv., 250·7. $C_{15}H_{28}O_2$ requires CO equiv., 240). The ketal was very unstable.

Oxidation of this ketal at 100—110° led to rapid formation of peroxide (25% in 1½ hr.), but this decomposed even more rapidly (to 6% in a further ½ hr.), and the peroxide could not be isolated. The oxidation products identified were *cyclo*hexanol, *cyclo*hexanone, *cyclo*hexyl formate and acetate, and adipic acid.

The author thanks Mr. D. J. G. Long for preparation of the *cyclo*hexyl methyl ether and the Directors of the Distillers Co. Ltd. for permission to publish this paper.

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The Stabilities of Metal Chelate Compounds formed by Some Heterocyclic Acids. Part II. Studies in Aqueous Dioxan.*

By F. HOLMES and W. R. C. CRIMMIN.

[Reprint Order No. 6447.]

Stability constants are reported for some chelated compounds with metals formed by picolinic, 6-methylpicolinic, and quinoline-2- and -8-carboxylic acid in 50% (v/v) dioxan–water, the method used being that of potentiometric titration. The results conform with those previously obtained in aqueous solution, although not always exactly.

IN Part I* stoicheiometric stability constants were reported for chelated compounds formed by a few metals with picolinic, 6-methylpicolinic, and quinoline-2- and -8-carboxylic acid in aqueous solution. Where the solubility of the complexes permits, the evaluation of stability data in such a medium rests on a sounder theoretical foundation than when solvents such as dioxan–water mixtures must be used. Since in our case some of the complexes were but slightly soluble in water, stability constants were also obtained in 50% (v/v) dioxan–water. Although the interpretation of data from this medium is uncertain, much useful information may be obtained by making assumptions as to the corrections to be employed. Such corrections have been made, especially by Van Uitert and Haas (*J. Amer. Chem. Soc.*, 1953, **75**, 451), but the corrections we have used rest on a rather different theoretical foundation, although they lead to quantitatively similar results. One of the main difficulties is that of interpreting pH meter readings in such a medium. The situation, as far as effective ionic concentrations is involved, is markedly changed by the non-polar solvent, and in particular the approximation $[H^+] = a_{H^+}$, justifiable in dilute aqueous solution, can no longer be used. The Debye–Hückel limiting law or the comprehensive data of Harned and Owen ("Physical Chemistry of Electrolytic Solutions," Reinhold Publ. Corp., New York, 29th edn.) could be used to correct for the increases in association, both for the hydrogen ion and for the other factors necessary in the calculations of $\bar{n}$ and $[L^-]$; this would lead to thermodynamic stability constants, but the corrections are not readily made, especially when metal ions are involved. No advantage would be gained in the present work by attempting to derive such thermodynamic data, especially when the figures obtained in water previously were stoicheiometric.

There is need, however, for calibrating the electrode system. Van Uitert and Haas (*loc. cit.*) have shown, by using a cell consisting of a hydrogen electrode and a silver–silver

* Part I, *J.*, 1955, 1175.

chloride electrode, that the glass–calomel cell used in titrations measures hydrogen-ion activity as defined by a hydrogen electrode, an empirical calibration for one pH being valid over a wide range of hydrogen-ion concentrations under the same conditions of solvent mixture and ionic concentration. We have confirmed this.

If $(a_{H^+})_0$ is the hydrogen-ion activity given by the pH meter reading, and $(c_{H^+})_c$ is the stoicheiometric concentration assuming complete dissociation, we have found that

$$(a_{H^+})_0/\gamma_{H^+}(c_{H^+})_c = k = 1{\cdot}56 \pm 0{\cdot}03 \quad . \quad . \quad . \quad . \quad . \quad (1)$$

for our electrode system under the conditions of our titrations, and over a range of pH values. The values for γ were obtained by interpolation from Harned and Owen's data (*loc. cit.*).

As has been previously pointed out, the other terms in the equations used for calculating $\bar{n}$ and $[L^-]$ are in molarities. The hydrogen-ion term may be expressed similarly. From (1)

$$\gamma_{H^+}(c_{H^+})_c = (a_{H^+})_0/1{\cdot}56$$

$$\therefore \quad (c_{H^+})_c = (a_{H^+})_0/k'$$

$$\therefore \quad pH_c = pH_0 + k''$$

In the present work, $k'' = 0{\cdot}07$. This is clearly the correction to be added to the pH meter reading.

Following Irving and Rossotti's nomenclature (*J.*, 1954, 2907), the stability constants obtained by using this correction are termed " practical " constants.

Experimental and Results

Dioxan (B.D.H., " AnalaR " grade) was purified according to Weissberger and Proskauer (" Organic Solvents," Oxford Univ. Press, 1935).

The rest of the materials used were as in Part I (*loc. cit.*) and the potentiometric titrations were carried out as described there, except that the titrated solution contained 50% (v/v) of dioxan.

Results.—Non-thermodynamic ionisation exponents for the acids are given in Table 1. Previously, for work in aqueous solution, the first ionisation exponents were obtained spectro-

Table 1.

Acid	First iontn. exponent	Second iontn. exponent
Quinoline-8-carboxylic	<2	7·76
Quinoline-2-carboxylic	1·8	5·39
*iso*Quinoline-1-carboxylic	not detd.	5·46
Picolinic	~1·5	5·71
6-Methylpicolinic	<1	6·59

photometrically; in 50% dioxan–water this was no longer convenient, so approximate figures obtained by potentiometric titration were used and are quoted in Table 1. Although their use might in some cases cause slight error in the lower $\bar{n}$ values, the general conclusions reached are in no way invalidated.

Stability data for chelated complexes. Titration figures are given for complexes between copper and quinoline-8-carboxylic acid as an example in Table 2, so that the pH range over

Table 2.

Quinoline-8-carboxylic acid (0·0230 g.). Concn. of $HClO_4$: 0·0866N, concn. of NaOH: 0·1034N. Initial vol.: 68·4 ml.

NaOH, ml.	3·385	3·853	4·091	4·392	4·610	4·778	4·847	4·922	5·022	5·110
pH	2·89	3·04	3·15	3·35	3·55	3·74	3·84	3·98	4·20	4·47
$\bar{n}$	0·34	0·58	0·67	0·84	0·97	1·13	1·18	1·24	1·35	1·44
log $1/[L^-]$	7·80	7·76	7·63	7·48	7·32	7·19	7·12	7·01	6·83	6·79

which chelation takes place in dioxan–water may be compared with that given for water in Part I. It will be seen that once again complex formation takes place at low pH's, with the attendant difficulties discussed previously. Nevertheless stability constants have again been

taken as the values of log $1/[L^-]$ at $\bar{n} = \frac{1}{2}$, 1, and $1\frac{1}{2}$. In a number of cases constants have also been evaluated by the method of least squares as suggested by Irving and Rossotti (*J.*, 1953, 3397); the maximum difference between the two figures is less than 0·2, and in view of what was said in Part I concerning the accuracy of the results it has not been thought necessary to quote these constants.

For complexes other than that formed by copper and quinoline-8-carboxylic acid, only stability constants are quoted; these are given in Table 3. Figures in parentheses have been obtained from the equation log K_1 + log K_2 = log K_n, or occasionally by slight graphical extrapolation.

TABLE 3.

Metal	log K_1	log K_2	log K_n	Metal	log K_1	log K_2	log K_n
Quinoline-8-carboxylic acid				Picolinic acid			
Cu	7·8	—	14·7	Cu	—	6·6	—
Ni	6·2	5·2	11·4	Ni	(6·1)	6·1	12·2
Co	5·3	4·3	9·6	Co	(5·9)	5·4	11·3
Zn	4·9	(4·1)	9·0				
Pb	4·5	—	—	6-Methylpicolinic acid			
Mn	4·2	—	—	Cu	—	~8	—
				Ni	(7·4)	5·8	13·2
Quinoline-2-carboxylic acid				Co	(6·6)	5·6	12·1
Ni	5·3	5·0	10·4				
Co	5·3	4·8	10·2				
Zn	5·1	4·6	9·7				

*iso*Quinoline-1-carboxylic acid gave derivatives too insoluble for stability constants to be determined. With quinoline-2-carboxylic acid and copper a precipitate appeared at too low a pH for values to be obtained.

DISCUSSION

The first ionisation exponents of the parent acids are in the order quinoline-8-carboxylic = quinoline-2-carboxylic > picolinic > 6-methylpicolinic acid; and the second ionisation exponents in the order quinoline-8-carboxylic > 6-methylpicolinic > picolinic > quinoline-2-carboxylic acid. These, as expected, are the same as in aqueous solution. Hence the complexes formed by quinoline-8-carboxylic acid should be by far the most stable. This is not so, and both increased ring size and steric factors are probably effective in the reduction of stability, the first as may be seen by the fact that log K_1 is considerably lower than expected for both nickel and cobalt when compared with the corresponding values using picolinic acid, and the second because the spreading factor is very much smaller with this latter acid.

In the case of 6-methylpicolinic acid the spreading factor leaves no doubt of steric hindrance although, with both nickel and cobalt, log K_1 is greater than it is when picolinic acid is the chelating agent; the latter fact is not unexpected when second dissociation exponents are compared.

With quinoline-2-carboxylic acid the effect of the second dissociation exponent would be to make the complexes less stable than those of picolinic acid; in addition, steric hindrance due to the benzenoid ring might be expected although this is not obvious from the spreading factor. In fact, examination of models or the construction of scale diagrams shows the 6-methyl group to have a much greater steric effect than the 5 : 6-benzenoid ring so that the much lower spread with quinoline-2-carboxylic acid is not surprising.

It is not always possible, however, to rely on deductions made from the magnitude of the spreading factor. With the compounds we have studied it would be expected that the factor would be less for cobalt complexes, having tetrahedral configuration, than for nickel and copper compounds with a planar structure, the latter especially. Insufficient figures are given for copper compounds but the expectation is not borne out on comparing the nickel and cobalt derivatives. Neither is it in other cases quoted in the literature as may be seen, for example, in the figures for " oxine " complexes and related compounds given by Irving and Rossotti (*J.*, 1954, 2910) and in those of Freiser quoted in the same paper. It is possible, of course, that the nickel is tetrahedrally bonded, although it is not probable that such would be the case with copper.

One point which emerges from the figures is that behaviours in water and dioxan–water

are not exactly parallel; in particular, the values of log K_1 and log K_2 for the nickel and cobalt complexes are greater for picolinic than for 6-methylpicolinic acid in water, although this order is reversed in dioxan–water for log K_1 but not for log K_2. This behaviour is not unexpected in view of the comparatively large increase in the second dissociation exponent for 6-methylpicolinic acid in dioxan–water, but it does serve to underline Irving's warning (*Analyst*, 1952, **77**, 841) that it may not be possible always to correlate conclusions drawn from experiments in different media, or to assume that findings in one solvent are always true for another.

It may be noted that with each acid the stabilities of the chelated compounds studied follow the Irving–Williams order.

Grateful acknowledgment is made to the University College of North Wales and the Ministry of Education for a postgraduate award to one of us (W. R. C. C.), to Professor S. Peat, F.R.S., for his encouragement, and to the Chemical Society for a grant for the purchase of a pH meter.

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The Reaction of Diazonium Salts with α-Aceto-γ-lactones.

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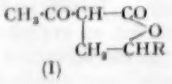
α-Aceto-γ-butyrolactone (I; R = H) reacts with two mols. of an aromatic diazonium salt in strongly alkaline solution to give a 1 : 5-diaryl-3-2′-hydroxyethylformazan (III; R = R′ = H) or a 1-aryl-3-arylazo-Δ²-pyrazoline (V) depending on whether the aryl group contains an *ortho*-substituent. α-Oxo-γ-butyrolactone arylhydrazones (II; R = H) are intermediate in the formation of either type of product but the corresponding acids (VI) give only the formazans.

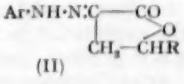
α-Aceto-γ-valerolactone gives only the 1 : 5-diaryl-3-2′-hydroxypropylformazans (III; R = Me, R′ = H).

THE reaction of benzenediazonium salts with α-aceto-γ-butyrolactone (I; R = H) in neutral or weakly alkaline solution is known to give the pale yellow α-oxo-γ-butyrolactone phenylhydrazone (II; R = H, Ar = Ph) (Harradence and Lyons, *J. Proc. Roy. Soc. New South Wales*, 1938, **72**, 221; Feofilaktow and Onischenko, *J. Gen. Chem. U.S.S.R.*, 1939, **9**, 304).

Addition of arenediazonium salts to α-aceto-γ-butyrolactone in strongly alkaline solution at 0—5° gave orange or red products, which were usually precipitated in the crude state as dark tars. Filtration, followed by lixiviation with methanol, gave substantially pure materials which were the result of the interaction of two mols. of the diazonium salt with one of the lactone, and at high pH were the main products even if only one equivalent of the diazonium compound was added (cf. Walker, *J.*, 1923, 2776). The nature of the final product depended upon the aryl group of the diazonium salt, and, of those studied, only that from *p*-nitroaniline failed to give a pure material.

Diazonium salts from *ortho*-substituted anilines gave 3-2′-hydroxyethylformazans (III; R = R′ = H). The type of *ortho*-substituent appeared to have no effect as formazans were obtained from *o*-toluidine, *o*-anisidine, *o*-bromoaniline, and *o*-chloroaniline.


(I)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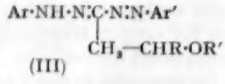
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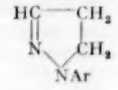
The same products were obtained by treating the arylhydrazones (II; R = H) with diazonium salts in alkaline solution, showing that the hydroxy-acid (VI) is an intermediate stage in the formation of the formazan. An unsymmetrical formazan (III; R = R′ = H, Ar = *o*-tolyl, Ar′ = *o*-chlorophenyl) was prepared by the latter process

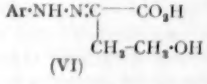
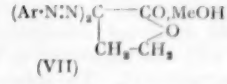
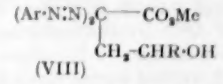
and the same product was obtained when either (II; R = H, Ar = *o*-tolyl) or (II; R = H, Ar = *o*-chlorophenyl) was the starting material. This proves that both the arylazo-groups have entered at the α-carbon atom of the lactone and establishes the structure of the formazans. With acetic anhydride, the formazans gave acetyl derivatives and, as 3-methyl-1 : 5-diphenylformazan was unaffected by such treatment, these compounds must be 3-2′-acetoxyethylformazans (III; R = H, R′ = Ac).

α-Aceto-γ-butyrolactone and aromatic diazonium salts free from *ortho*-substituents gave noticeably paler products, which gave no acetyl derivatives, were identical with the

(IV)  (V)

compounds obtained by treating 1-aryl-Δ^2-pyrazolines (IV) in acetic acid with the appropriate diazonium salts and must therefore be 1-aryl-3-arylazo-Δ^2-pyrazolines (V) (Duffin and Kendall, *J.*, 1954, 408).

Although the arylhydrazones (II; R = H) must be intermediates in the formation of the 3-arylazo-Δ^2-pyrazolines, a number of experiments in which a diazonium salt was added to an alkaline *solution* of the hydrazone (II) (both aryl groups being free from *ortho*-substituents) failed to give any isolatable product. However, addition of benzenediazonium chloride to a *suspension* of α-oxo-γ-butyrolactone phenylhydrazone (II; Ar = Ph, R = H) in 10% aqueous sodium hydroxide gave 1-phenyl-3-phenylazo-Δ^2-pyrazoline (V; Ar = Ph); and diazotised *p*-bromoaniline and alkaline *solution* of α-oxo-γ-butyrolactone *p*-bromophenylhydrazone (II; Ar = *p*-bromophenyl, R = H) gave, not the pyrazoline (V; Ar = *p*-bromophenyl) as obtained from a *suspension* of these reactants, but 1 : 5-di-*p*-bromophenyl-3-2′-hydroxyethylformazan (III; Ar = Ar′ = *p*-bromophenyl, R = H). It appears that isolation of the product in the latter case was aided by its rather low solubility. Therefore, the action of a diazonium salt on the salt of α-oxo-γ-hydroxybutyric acid arylhydrazone (VI) gives the formazan (III) and that with the α-oxo-γ-lactone arylhydrazone gives the 3-arylazo-Δ^2-pyrazoline (V). This was supported by experiments in which diazotised *o*-toluidine and *o*-chloroaniline were condensed with α-aceto-γ-butyrolactone in the presence of the minimum quantity of alkali required to introduce two arylazo-groups, *i.e.*, under conditions in which opening of the lactone ring would be least likely. The products were not the formazans but gave analyses for $C_{19}H_{22}O_3N_4$ and $C_{19}H_{16}O_3N_4Cl_2$ respectively. Either hot alcoholic sodium hydroxide or hydrochloric acid converted these materials into 1-aryl-3-arylazo-Δ^2-pyrazolines (V). There are therefore two possible structures for these substances, namely (VII) or (VIII; R = H); the latter was preferred as attempts to remove the " methanol of crystallization "

 (VI)  (VII)  (VIII)

at 80° *in vacuo* resulted in decomposition. The use of ethanol for lixiviation during the isolation of the products was a failure as the materials were too soluble in this solvent. It was further noted that the lixiviation of a crude product from which a pyrazoline was finally obtained was exothermic and of that from which a formazan was obtained was not so. By the method used for isolation, small quantities of alkali must be transferred to the methanol with the crude product and the formation of (VIII; R = H) would appear to be alkali-catalysed, as is the formation of very similar products from arylazomalonyl-2-aminopyridines (Snyder and Robison, *J. Amer. Chem. Soc.*, 1952, **74**, 4910). In a series of experiments, acetic acid was added to the methanol to prevent any alkaline-catalysed reaction at this stage and two important results were obtained. Those reactions which gave formazans (III) were unaffected whereas the crude products from those reactions which would have given pyrazolines (V) gave instead only the α-oxo-γ-butyrolactone arylhydrazones (II; R = H). It is therefore suggested that the pyrazolines are formed by the initial formation of the lactone (VII) in the coupling stage which is then converted,

in the alkaline methanol, into the ester (VIII; R = H) and, if Ar is not *ortho*-substituted, this gives, at room temperature, the final pyrazoline (V) whereas the absence of alkali in the methanol results in the decomposition of bisdiazo-lactone (VII) to the hydrazone (II). The formation of the formazans is seen as the action of the diazonium salt on the sodium salt of the hydrazono-acid (VI) with simultaneous expulsion of the carboxyl group. The *ortho*-substituent may act by assisting the opening of the lactone ring.

α-Aceto-γ-valerolactone (I; R = Me) gave the arylhydrazones (II; R = Me) but the introduction of the second arylazo-group was very slow and from most experiments only the hydrazones (II; R = Me) were obtained even at high pH. The formazan (III; Ar = *o*-chlorophenyl, R = Me) was, however, obtained in good yield, and diazotized *o*-toluidine gave the ester (VIII; Ar = *o*-tolyl, R = Me) which gave no pyrazoline on treatment with hot alcoholic alkali.

Experimental

α-Oxo-γ-lactone Arylhydrazones.—The following exemplifies the procedure: *o*-Toluidine (5·0 ml.) in 5N-hydrochloric acid (25 ml.) was diazotized at 0—5° by sodium nitrite (3·5 g.) in water (10 ml.) with stirring. This solution was added to α-aceto-γ-butyrolactone (6·0 ml.) in water (25 ml.) and pyridine (25 ml.) at 5°. After 1 hr., the precipitated solid was filtered off and recrystallized from acetic acid to give light yellow *α-oxo-γ-butyrolactone o-tolylhydrazone*, m. p. 178° (6·5 g., 64%) (Found: C, 64·6; H, 6·1. $C_{11}H_{12}O_2N_2$ requires C, 64·7; H, 5·9%). Similar experiments are summarized in Table 1.

Table 1. *α-Oxo-γ-lactone arylhydrazones* (II).

Ar	R	Yield (%)	M. p.	Found (%) C	Found (%) H	Formula	Required (%) C	Required (%) H
Ph	H	77	228°	63·2	5·1	Kletz and Lapworth, *J.*, 1915, 1262.		
o-C_6H_4Cl	H	63	145 [b]	53·35	3·8	$C_{10}H_9O_2N_2Cl$	53·45	4·0
o-$C_6H_4{\cdot}NO_2$	H	52	237 [d]	50·9	3·75	$C_{10}H_9O_4N_3$	51·11	3·85
p-C_6H_4Br	H	75	257 [d]	44·7	3·65	$C_{10}H_9O_2N_2Br$	44·7	3·35
Ph	Me	49	199 [c]	64·5	6·0	$C_{11}H_{12}O_2N_2$	64·7	5·9
o-C_6H_4Cl	Me	80	162 [c]	55·2	4·35	$C_{11}H_{11}O_2N_2Cl$	55·4	4·6

[a] Pale yellow leaflets from ethanol. [b] Yellow needles from methanol. [c] Yellow needles from ethanol. [d] Yellow needles from 2-methoxyethanol.

α-Oxo-γ-hydroxybutyric Acid Phenylhydrazone.—α-Oxo-γ-butyrolactone phenylhydrazone (5 g.) was heated at 100° for 10 min. with 10% aqueous sodium hydroxide (20 ml.). The solution was filtered and cooled to 0°, and 10N-hydrochloric acid (6 ml.) was added to precipitate the *acid* as colourless leaflets which, dried *in vacuo*, had m. p. 156° (4·8 g., 88%). Very rapid recrystallization from water failed to raise the m. p. (Found: C, 57·5; H, 5·5. $C_{10}H_{12}O_3N_2$ requires C, 57·5; H, 5·7%) but prolonged boiling with water or, better, treatment with ethanolic hydrogen chloride at 0°, gave the lactone again.

3-2′-Hydroxyalkylformazans.—The following exemplify the procedures: (A) *From the α-aceto-γ-lactone.* *o*-Toluidine (2·6 ml.) was diazotized in 5N-hydrochloric acid (12·5 ml.) at 5° with sodium nitrite (1·8 g.) in water (8 ml.). The solution was added dropwise to a stirred solution of α-aceto-γ-butyrolactone (1·6 ml.) in 10% aqueous sodium hydroxide (45 ml.) and ice (110 g.). After 1 hr., the precipitated red tar was filtered off and lixiviated with methanol (2 × 25 ml.), to leave a mass of brownish crystals. Recrystallization from methanol gave *3-2′-hydroxyethyl-1:5-di-o-tolylformazan* as orange needles, m. p. 145° (1·24 g., 34%) (Found: C, 69·2; H, 6·75. $C_{17}H_{20}ON_4$ requires C, 68·9; H, 6·95%). Similar experiments are summarized in Table 2.

Table 2. *3-2′-Hydroxyalkylformazans* (III, R′ = H) (*Method A*).

Ar = Ar′	R	Yield (%)	M. p. [a]	Found (%) C	Found (%) H	Formula	Required (%) C	Required (%) H
o-C_6H_4Cl	H	40	147° [c]	53·5	4·2	See above		
o-C_6H_4Br	H	10	157 [c]	42·3	3·5	$C_{15}H_{14}ON_4Br_2$	42·4	3·3
o-$C_6H_4{\cdot}OMe$ ...	H	12	133 [b]	61·15	5·95	$C_{17}H_{20}O_2N_4$	62·2	6·1
o-C_6H_4Cl	Me	17 [d]	124 [c]	54·6	4·6	$C_{16}H_{14}ON_4Cl_2$	54·7	4·55

[a] From MeOH. [b] Dark red needles with green reflex. [c] Red needles with blue reflex. [d] Orange-red needles. [e] With α-oxo-γ-valerolactone *o*-chlorophenylhydrazone (28%).

(B) *From the arylhydrazone.* α-Oxo-γ-butyrolactone *o*-chlorophenylhydrazone (11·2 g.) was dissolved, by warming, in 10% aqueous sodium hydroxide (90 ml.). The solution was cooled and *o*-chlorobenzenediazonium chloride solution [from *o*-chloroaniline (5·3 ml.), 5N-hydrochloric acid (25 ml.) and sodium nitrite (3·5 g.) in water (15 c.c.)] added gradually during 1 hr. at 0°. After 60 hr., the precipitated red solid was filtered off, washed with methanol, and recrystallized from the same solvent, to give 1 : 5-*di*-o-*chlorophenyl*-3-2′-*hydroxyethylformazan* as red needles with a green reflex, m. p. 147° (6·5 g., 38%) (Found: C, 53·4; H, 4·3; Cl, 21·0. $C_{15}H_{14}ON_4Cl_2$ requires C, 53·5; H, 4·2; Cl, 21·1%). Similar experiments are summarized in Table 3.

TABLE 3. 3-2′-*Hydroxyalkylformazans* (III; R′ = H) (*Method B*).

Arylhydrazone (II) Ar	R	Diazonium cpd.	Yield (%)	M. p.	Found (%) C	H	Formula	Required (%) C	H
o-C_6H_4·NO_2	H	*o*-NO_2·C_6H_4·N_2	4 [a]	162°	50·5	4·2	$C_{15}H_{14}O_3N_6$	50·2	3·9
o-C_6H_4Me	H	*o*-C_6H_4Cl·N_2	23 [b]	140	60·2	5·35	$C_{16}H_{17}ON_4Cl$	60·5	5·35
o-C_6H_4Cl	H	*o*-C_6H_4Me·N_2	7 [b]	140	60·4	5·45			
o-C_6H_4Cl	Me	*o*-C_6H_4Cl·N_2	15 [c]	125	54·5	4·5	See above		
Ph	Me	Ph·N_2	4 [d]	108					

[a] Red needles from MeOH. [b] Dark red needles with green reflex from MeOH. [c] Orange-red needles from MeOH. [d] Dark red needles with blue reflex from light petroleum. Found: N, 19·7. $C_{16}H_{18}ON_4$ requires N, 19·85%.

3-2′-*Acetoxyethyl*-1 : 5-*di*-o-*chlorophenylformazan*.—1 : 5-Di-*o*-chlorophenyl-3-2′-hydroxyethylformazan (0·5 g.), benzene (10 ml.), and acetic anhydride (2 ml.) were warmed on a water-bath for 10 min. and ethanol (10 ml.) added. Evaporation gave reddish crystals which were recrystallized from methanol, to give 3-2′-*acetoxyethyl*-1 : 5-*di*-o-*chlorophenylformazan* as red needles with a green reflex, m. p. 120° (0·15 g., 28%) (Found: C, 53·54; H, 4·2; Cl, 19·1. $C_{17}H_{16}O_2N_4Cl_2$ requires C, 53·7; H, 4·2; Cl, 18·8%). Similar treatment of 3-methyl-1 : 5-diphenylformazan gave unchanged material (92%). The following acetoxy-compounds were prepared from the appropriate formazans: 3-2′-*acetoxyethyl*-1 : 5-*di*-o-*tolylformazan* from methanol as orange plates, m. p. 118° (Found: C, 67·4; H, 6·6. $C_{19}H_{22}O_2N_4$ requires C, 67·5; H, 6·5%), 3-2′-*acetoxyethyl*-1 : 5-*di*-o-*bromophenylformazan* from ethanol as red needles, m. p. 121° (Found: Br, 34·0. $C_{17}H_{16}O_2N_4Br_2$ requires Br, 34·2%), 3-2′-*acetoxyethyl*-1 : 5-*di*-o-*nitrophenylformazan* from ethanol as red needles, m. p. 129° (Found: C, 51·1; H, 3·7. $C_{17}H_{16}O_6N_6$ requires C, 51·0; H, 4·0%), 3-2′-*acetoxyethyl*-1 : 5-*di*-o-*methoxyphenylformazan* from aqueous methanol as red needles, m. p. 97° (Found: C, 61·4; H, 4·9. $C_{19}H_{22}O_4N_4$ requires C, 61·7; H, 4·95%), and 3-2′-*acetoxypropyl*-1 : 5-*di*-o-*chlorophenylformazan* from methanol as orange plates, m. p. 117° (Found: Cl, 18·1. $C_{18}H_{18}O_2N_4Cl_2$ requires Cl, 18·05%).

1-*Aryl*-3-*arylazo*-Δ²-*pyrazolines*.—The following exemplifies the procedure: Aniline (4·65 g.) in 5N-hydrochloric acid (25 ml.) was diazotized at 5—10° with sodium nitrite (3·5 g.) in water (10 ml.) and then added with stirring to a solution of α-aceto-γ-butyrolactone (3·5 ml.) in 10% aqueous sodium hydroxide (80 ml.) during 30 min. After 1 hr. the precipitated red tar was filtered off and left for 16 hr. with methanol (50 ml.). The resulting orange crystals, recrystallized from methanol, gave 1-phenyl-3-phenylazo-Δ²-pyrazoline as orange leaflets, m. p. 156° (1·5 g., 24%) (Duffin and Kendall, *loc. cit.*) (Found: C, 71·95; H, 5·5. Calc. for $C_{15}H_{14}N_4$: C, 72·0; H, 5·6%). Similar experiments are summarized in Table 4.

TABLE 4. 1-*Aryl*-3-*arylazo*-Δ²-*pyrazolines* (V).

Ar	M. p.*	Yield (%)	Found (%) C	H	Formula	Required (%) C	H
m-C_6H_4Me	150°	23	73·3	6·3	Duffin and Kendall, *loc. cit.*		
p-C_6H_4Me	184	10	73·45	6·6			
p-C_6H_4·OMe	194	24	65·8	6·00	$C_{17}H_{18}O_2N_4$	65·8	5·8
p-C_6H_4Br	206	30	43·8	2·8	$C_{15}H_{12}N_4Br_2$	44·0	2·9
m-C_6H_4Cl	135	32	56·7	3·8	$C_{15}H_{12}N_4Cl_2$	56·4	3·8

* The products form red needles, except the first and fourth which form orange plates; all were crystallized from methanol, except the third and fourth which crystallized from benzene.

Methyl γ-*Hydroxy*-αα-*di*-o-*tolylazobutyrate*.—*o*-Toluidine (2·6 ml.) was diazotized in 5N-hydrochloric acid (12·5 ml.) at 5—10° with sodium nitrite (1·8 g.) in water (5 ml.) and added slowly to a stirred solution of α-aceto-γ-butyrolactone (1·6 ml.) in 10% aqueous sodium hydroxide (25 ml.) at 0—5°. After 1 hr., the precipitated tar was filtered off and lixiviated with methanol (2 × 25 ml.) to give the *azo-compound* as red needles with a green reflex, m. p. 98·5° (2·03 g.,

46%); recrystallization from methanol or light petroleum did not change the m. p. [Found: C, 64·4; H, 6·3; N, 16·0%; *M* (ebullioscopic in benzene), 341. $C_{19}H_{22}O_3N_4$ requires C, 64·4; H, 6·25; N, 15·8%; *M*, 354]. By similar processes, *o*-chloroaniline and α-aceto-γ-butyrolactone gave *methyl αα-di-o-chlorophenyl-γ-hydroxybutyrate* as light red needles (from light petroleum), m. p. 91° (15%) (Found: C, 51·8; H, 4·23; Cl, 18·0. $C_{17}H_{16}O_3N_4Cl_2$ requires C, 51·7; H, 4·0; Cl, 18·0%); and *o*-toluidine and α-aceto-γ-valerolactone gave *methyl γ-hydroxy-αα-di-o-tolylazovalerate* as red needles with green reflex, m. p. 82° (30%) [Found: C, 65·25; H, 6·45; N, 15·4%; *M* (ebullioscopic in benzene), 356. $C_{20}H_{24}O_3N_4$ requires C, 65·2; H, 6·5; N, 15·2%; *M*, 368].

1-*o*-*Tolyl*-3-*o*-*tolylazo*-Δ²-*pyrazoline*.—Methyl γ-hydroxy-αα-di-*o*-tolylazobutyrate (0·5 g.) was dissolved in ethanol (20 ml.), and 40% aqueous sodium hydroxide (1 ml.) added. After 1 hour's boiling during which the colour changed from violet to orange-yellow, water (100 ml.) was added and the precipitated solid filtered off. Recrystallization from methanol gave 1-*o*-tolyl-3-*o*-tolylazo-Δ²-pyrazoline as red needles, m. p. 92·5° (0·09 g., 25%) (Found: C 73·4; H, 6·6. Calc. for $C_{17}H_{18}N_4$: C, 73·3; H, 6·45%) (Duffin and Kendall, *loc. cit.*). A similar experiment in which the sodium hydroxide was replaced by 10N-hydrochloric acid gave the same product (31%). By similar methods, methyl αα-di-*o*-chlorophenylazo-γ-hydroxybutyrate gave 1-*o*-*chlorophenyl*-3-*o*-*chlorophenylazo*-Δ²-*pyrazoline* as red needles, m. p. 95° (28%) (Found: C, 56·5; H, 3·7; Cl, 22·35. $C_{15}H_{12}N_4Cl_2$ requires C, 56·5; N, 3·8; Cl, 22·3%), but no pure product was obtained from methyl γ-hydroxy-αα-di-*o*-tolylazovalerate.

Experiments on Mechanism of the Reaction.— (*a*) Aniline (0·93 g.) was diazotized in 5N-hydrochloric acid (5·0 ml.) with sodium nitrite (0·75 g.) in water (3 ml.). α-Oxo-γ-butyrolactone phenylhydrazone (1·9 g.) was suspended in 10% aqueous sodium hydroxide (15 ml.) at 0° and the diazonium solution added slowly. After 2 hr. the mixture was diluted with water (100 ml.) and the precipitated tar filtered off. After 60 hr. in methanol, a mass of orange crystals was filtered off and recrystallized from methanol, to give 1-phenyl-3-phenylazo-Δ²-pyrazoline, m. p. 156° (0·30 g., 12%) (Found: C, 71·6; H, 5·7%). A similar experiment in which the lactone was dissolved in warm alkali and then cooled to 0° before coupling gave no pure product.

(*b*) In a similar manner *p*-bromoaniline and α-oxo-γ-butyrolactone *p*-bromophenylhydrazone gave 1-*p*-bromophenyl-3-*p*-bromophenylazo-Δ²-pyrazoline (11%) identical with the product obtained previously.

(*c*) *p*-Bromoaniline (3·45 g.) in 3N-hydrochloric acid (15 ml.) was diazotized at 0—5° with sodium nitrite (1·5 g.) in water (5 ml.) and then added to a solution (prepared by warming) of α-oxo-γ-butyrolactone *p*-bromophenylhydrazone (5·5 g.) in 4% aqueous sodium hydroxide (100 ml.) and ice (200 g.). After 1 hr., the precipitated solid was filtered off, washed with water, and lixiviated with methanol (2 × 25 ml.) to give an orange solid. Recrystallization from benzene gave 1 : 5-*di*-p-*bromophenyl*-3-2′-*hydroxyethylformazan* as orange needles, m. p. 152° (2·05 g., 24%) (Found: C, 42·2; H, 3·4. $C_{15}H_{14}ON_4Br_2$ requires C, 42·4; H, 3·3%).

(*d*) *m*-Toluidine (5·3 ml.) in 5N-hydrochloric acid (25 ml.) was diazotized at 0—5° with sodium nitrite (3·5 g.) in water (10 ml.) and added with stirring to a solution of α-aceto-γ-butyrolactone (3·5 ml.) in 10% aqueous sodium hydroxide (60 ml.) at 0—5°. After 1 hr., the precipitated solid was filtered off and added to a mixture of methanol (50 ml.) and acetic acid (2 ml.). The initial red colour became rapidly paler and after 15 hr. a pale yellow solid was present. Filtration and recrystallization from ethanol gave *α-oxo-γ-butyrolactone m-tolylhydrazone* (3·3 g., 65%) as yellow leaflets, m. p. 197° (Found: C, 64·5; H, 6·0. $C_{11}H_{12}O_2N_2$ requires C, 64·7; H, 5·9%). Similarly, α-aceto-γ-butyrolactone with *p*-bromoaniline gave the hydrazone (II; R = H, Ar = *p*-bromophenyl), and with *o*-chloroaniline the formazan (III; R = R′ = H, Ar = *o*-chlorophenyl).

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*Hydroxycarbazoles and Tetrahydrohydroxycarbazoles. Part III.**

By José A. Cummins and Muriel L. Tomlinson.

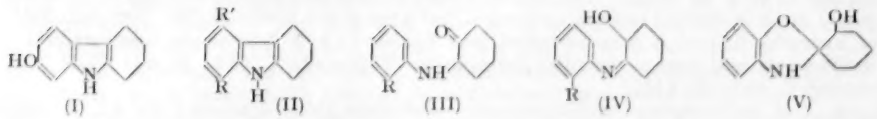
[Reprint Order No. 6456.]

The hitherto unknown 4-hydroxy-, 4-methoxy-, and 1 : 2 : 3 : 4-tetrahydro-5-methoxy-carbazole are described. The compound previously described as 1 : 2 : 3 : 4-tetrahydro-7(or 5)-hydroxycarbazole is shown to be the 7-hydroxy-compound.

Jones and Tomlinson (*J.*, 1953, 4114) showed that 1 : 2 : 3 : 4-tetrahydro-7(or 5)-hydroxycarbazole (I), m. p. 163—164°, could be obtained from *m*-aminophenol and 2-hydroxy-*cyclo*hexanone. A substance, m. p. 164°, made from *cyclo*hexanone and *m*-hydroxyphenylhydrazine (D.R.P., 574,840; *Chem. Zentr.*, 1933, II, 622), has been described as the 7-hydroxy-compound but no proof of the position of the hydroxy-group appears to have been reported.

Authentic 1 : 2 : 3 : 4-tetrahydro-5-methoxycarbazole (II; R′ = OMe, R = H) has now been prepared by removing chlorine, by catalytic reduction, from 8-chloro-1 : 2 : 3 : 4-tetrahydro-5-methoxycarbazole (II; R′ = OMe, R = Cl) which was obtained by condensing 3-amino-4-chloroanisole with 2-hydroxy*cyclo*hexanone. This substance, m. p. 126—127°, is different from the methoxy-compound, m. p. 148—149°, prepared from Jones and Tomlinson's compound (I) which must therefore be 1 : 2 : 3 : 4-tetrahydro-7-hydroxycarbazole.

Dehydrogenation of 1 : 2 : 3 : 4-tetrahydro-7-hydroxycarbazole has yielded 2-hydroxycarbazole, m. p. 277°, most of the references to which are in patent literature (*e.g.*, B.P., 303,502; *Chem. Zentr.*, 1930, II, 470, which describes its preparation from 2-aminocarbazole and gives m. p. 276°). Hoshino and Takiura (*Bull. Chem. Soc. Japan*, 1936, **11**, 218) describe the preparation of 2-hydroxycarbazole, m. p. 273—274°, by dehydrogenation and dealkylation of the tetrahydrocarbazole which they obtained by the Fischer method from *cyclo*hexanone *m*-ethoxyphenylhydrazone. They give no evidence to prove that



it is the 2- and not the 4-hydroxy-compound. (See also B.P., 337,821; *Chem. Zentr.*, 1931, II, 1761.) The hitherto unknown 4-hydroxycarbazole has now been obtained by dehydrogenation of 1 : 2 : 3 : 4-tetrahydro-4-oxocarbazole and it has m. p. 169—170°. The product described by the Japanese authors is therefore proved to be 2-hydroxycarbazole.

It has now been found (compare Carter, Katritzky, and Plant, *J.*, 1955, 338) that condensation of aromatic amines with 2-hydroxy*cyclo*hexanone frequently proceeds in two stages. Infrared absorption spectra indicate that the intermediate compounds are 2-oxo*cyclo*hexylanilines (III) rather that the isomeric 2-hydroxy*cyclo*hexylideneanilines (IV). Condensation of *m*-aminophenol with 2-hydroxy*cyclo*hexanone proceeds exceptionally easily, without any catalyst, and no intermediate has been isolated. Moreover no trace of 4-methoxycarbazole could be found with the 2-methoxycarbazole prepared by methylating and dehydrogenating the crude reaction product. (The peroxidation which occurs rapidly in solution makes a search for the tetrahydro-5-methoxy-compound unsatisfactory.) 4-Methoxycarbazole has been prepared by removal of chlorine and hydrogen from the chloro-compound (II; R = Cl, R′ = OMe). The compound (III; R = OMe)

* *J.*, 1952, 2789, and *J.*, 1954, 1414, are regarded as Parts I and II.

prepared from *o*-anisidine, could not be converted into 1 : 2 : 3 : 4-tetrahydro-8-methoxycarbazole (II; R = OMe, R′ = H).

It is interesting to note that *o*-aminophenol condenses easily with 2-hydroxy*cyclo*hexanone (no catalyst) to give a substance, $C_{12}H_{15}O_2N$, which does not appear to be (III; R = OH). It does not react with sodium hydroxide, and consideration of its infrared absorption spectrum indicates that it may be 2-hydroxy*cyclo*hexane*spiro*benzoxazoline (V). It certainly contains no carbonyl group but it does give a ferric chloride reaction so the aniline (IV; R = OH) may not be ruled out.

1 : 2 : 3 : 4-Tetrahydro-5-methylcarbazole was prepared while using the chloro-compound (II; R = Cl, R′ = Me) as a model, before attempting to make the corresponding methoxy-compound. The m. p. and the rapid peroxidation recorded by Coldham, Lewis, and Plant (*J.*, 1954, 4528) were confirmed, and the substance has now been obtained analytically pure.

Experimental

1 : 2 : 3 : 4-*Tetrahydro-7-methoxycarbazole*.—1 : 2 : 3 : 4-Tetrahydro-7-hydroxycarbazole (1·3 g.) was methylated in acetone (12 c.c.) with methyl sulphate (1·8 g.) and sodium hydroxide (0·6 g. in a little water). The *ether* crystallised from ethanol as plates, m. p. 148—149° (Found: C, 77·7; H, 7·4. $C_{13}H_{15}ON$ requires C, 77·6; H, 7·4%).

3-*Amino*-4-*chloroanisole*.—4-Chloro-3-nitroanisole (32 g.), water (320 c.c.), iron powder (32 g.), and hydrochloric acid (4 c.c.) were boiled for 1½ hr., and after the mixture had been neutralised it was extracted with ether. The ethereal layer was extracted with dilute acid and the amine was again collected with ether from the basified aqueous extract. 3-*Amino*-4-*chloroanisole* (20·5 g.) distilled at 140—145°/18 mm. It solidified to an almost colourless mass of needles, m. p. 27° (Found: N, 9·1. C_7H_8ONCl requires N, 8·9%). With acetic anhydride it gave 3-*acetamido*-4-*chloroanisole* which separates from dilute acetic acid (50%) as needles, m. p. 99° (Found: C, 54·3; H, 5·3. $C_9H_{10}O_2NCl$ requires C, 54·1; H, 5·0%).

8-*Chloro*-1 : 2 : 3 : 4-*tetrahydro-5-methoxycarbazole*.—An intimate mixture of 3-amino-4-chloroanisole (1·0 g.), 2-hydroxy*cyclo*hexanone (0·72 g.), and a trace of the amine hydrochloride was heated at 120—125°. Recrystallisation from ethanol of the mass formed gave 4-*chloro*-3-2′-*oxo*cyclo*hexylaminoanisole* as needles, m. p. 72° (Found: C, 61·7; H, 6·3. $C_{13}H_{16}O_2NCl$ requires C, 61·5; H, 6·3%). The infrared spectra showed max. at 2·96 and 5·84 μ. The compound could be distilled *in vacuo* unchanged, but when it was heated at 190—200° with a drop of hydrochloric acid it was converted into 8-*chloro*-1 : 2 : 3 : 4-*tetrahydro-5-methoxycarbazole* which crystallised from methanol as plates, m. p. 99° (Found: C, 66·3; H, 6·1. $C_{13}H_{14}ONCl$ requires C, 66·2; H, 5·9%).

1 : 2 : 3 : 4-*Tetrahydro-5-methoxycarbazole*.—The above chloro-compound (0·5 g.), in methyl alcohol (50 c.c.) containing potassium hydroxide (0·5 g. in a little water), was shaken in hydrogen with palladium–charcoal (Norite containing 10% of palladium). Hydrogen (approx. 50 c.c.) was absorbed. The solution was filtered and diluted with water, and the precipitate was rapidly recrystallised from aqueous ethanol, from which 1 : 2 : 3 : 4-*tetrahydro-5-methoxycarbazole* separated as plates, m. p. 126—127°, sintering at 121°, and depressed by admixture with the above 7-methoxy-compound (Found: C, 77·7; H, 7·4. $C_{13}H_{15}ON$ requires C, 77·6; H, 7·5%).

1 : 2 : 3 : 4-*Tetrahydro-5-methylcarbazole*.—This was prepared in the same way from the corresponding methyl compound and was obtained from aqueous ethanol as plates, m. p. 147°, sintering at 140° (Found: 84·1; H, 8·1. $C_{13}H_{15}N$ requires C, 84·3; H, 8·1%).

1-*Chloro*-4-*methoxycarbazole*.—The corresponding tetrahydro-compound (2·0 g.) was refluxed with chloranil (4·0 g.) in sulphur-free xylene for 6 hr. The cooled solution was filtered from tetrachloroquinone, diluted with ether, and washed with sodium hydroxide. The residue left after solvents had been removed was dissolved in benzene and light petroleum (equal parts) and passed through activated alumina. 1-*Chloro*-4-*methoxycarbazole*, obtained from this solution, crystallised from light petroleum (b. p. 60—80°) as plates, m. p. 100—101° (Found: C, 67·4; H, 4·3. $C_{13}H_{10}ONCl$ requires C, 67·4; H, 4·3%).

4-*Hydroxycarbazole*.—1 : 2 : 3 : 4-Tetrahydro-4-oxocarbazole (1·0 g.), mixed with palladium–charcoal (0·5 g. containing 10% of palladium), was heated at 270° in carbon dioxide for 1 hr. A small quantity of carbazole sublimed and the main product was extracted from the charcoal with sodium hydroxide solution (4%). Acidification afforded 4-*hydroxycarbazole* which was

recrystallised from water containing a little hydrochloric acid. It separated as almost colourless needles, m. p. 169—170° (with blackening) (Found : C, 78·5; H, 5·1. $C_{12}H_9ON$ requires 78·7; H, 4·9%). It gives a violet ferric chloride reaction. 1-Hydroxycarbazole, m. p. 160—162° (together with a little carbazole), was obtained from similar treatment of 1 : 2 : 3 : 4-tetrahydro-1-oxocarbazole at 245° (Found : C, 78·9; H, 4·9. Calc. for $C_{12}H_9ON$: C, 78·7; H, 4·9%). In aqueous alcohol it gives a green precipitate with ferric chloride.

2-*Hydroxycarbazole*.—Similar dehydrogenation of 1 : 2 : 3 : 4-tetrahydro-7-hydroxycarbazole gave 2-hydroxycarbazole, m. p. 277° (black liquid and previous darkening) (Found, in sample dried *in vacuo* at 125° : C, 78·7; H, 4·9. Calc. for $C_{12}H_9ON$: C, 78·7; H, 4·9%).

4-*Methoxycarbazole*.—8-Chloro-1 : 2 : 3 : 4-tetrahydro-5-methoxycarbazole (0·7 g.) was dehydrogenated as above in carbon dioxide at 200—210° for 30 min. Hydrogen was then substituted for carbon dioxide and the temperature was raised to 240—250° for a further 30 min. Hydrogen chloride was evolved. The product was extracted with benzene, and the solution, diluted with an equal volume of light petroleum (b. p. 60—80°), was passed through activated alumina. From a band which showed greenish-yellow fluorescence in ultraviolet light, a solid was isolated; it crystallised from ethanol giving prisms of 4-*methoxycarbazole*, m. p. 135° (Found : C, 78·7; H, 5·7. $C_{13}H_{11}ON$ requires C, 79·2; H, 5·6%). (More vigorous dehydrogenation converted both 1-chloro-4-methoxycarbazole and the corresponding tetrahydro-compound into carbazole.)

2-*Methoxycarbazole*.—*m*-Aminophenol (2·2 g.) and 2-hydroxy*cyclo*hexanone (2·3 g.) were heated at 125—135°. The solid which resulted was methylated in acetone solution. Water precipitated the product, and the dried, crude, tetrahydromethoxycarbazole thus prepared was dehydrogenated as above at 180—200° in carbon dioxide. When the benzene extract of the product was diluted with an equal amount of light petroleum (b. p. 60—80°) 2-*methoxycarbazole* separated. It crystallised from alcohol as needles, m. p. 234° (Found : C, 79·0; H, 5·7. $C_{13}H_{11}ON$ requires C, 79·2; H, 5·6%). The mother liquor was passed through activated alumina which was then eluted with benzene and light petroleum until the alumina ceased to fluoresce in ultraviolet light. More 2-methoxycarbazole was isolated but no 4-methoxycarbazole was found.

2-2′-*Oxo*cyclo*hexylaminoanisole*.—*o*-Anisidine (1·0 g.) and 2-hydroxy*cyclo*hexanone (1·0 g.) reacted at 140—145° to give 2-2′-*oxo*cyclo*hexylaminoanisole* which crystallised from alcohol as plates, m. p. 72—74° (Found : C, 71·1; H, 7·8. $C_{13}H_{17}O_2N$ requires C, 71·2; H, 7·7%). Infrared spectrum showed bands at 2·97 and 5·86 μ. Similarly, *o*-aminophenol and 2-hydroxy-*cyclo*hexanone reacted at 135—140° to give a solid which crystallised from alcohol as plates, m. p. 171° (Found : C, 70·5; H, 7·3. $C_{12}H_{15}O_2N$ requires C, 70·2; H, 7·3%). Infrared spectrum showed bands at 2·93, 3·02, 3·09, 3·32, 3·77 μ and a number of big bands usually ascribed to $\rangle C{-}O{-}C$ in the 8—10 μ region. There was no band indicative of a carbonyl group. The substance may therefore be 2-*hydroxy*cyclo*hexane*spiro*benzoxazoline*. It forms a sparingly soluble hydrochloride that can be recrystallised from dilute hydrochloric acid. It gives a greenish-black colour with ferric chloride in aqueous alcohol and it can be recrystallised, unchanged, from aqueous sodium hydroxide solution.

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Pyrimidines. Part VIII. Halogeno- and Hydrazino-pyrimidines.*

By J. Chesterfield, J. F. W. McOmie, and E. R. Sayer.

[Reprint Order No. 6486.]

The only three previously unknown chloropyrimidines, namely 4 : 5-dichloro-, 2 : 4 : 5-trichloro-, and 4 : 5 : 6-trichloro-pyrimidine, have now been prepared together with 5-bromo-4 : 6-dichloropyrimidine. 5-Bromo-4-chloropyrimidine has been made by a new route.

Some reactions of these compounds with nucleophilic reagents including hydrazine are recorded and the results of bacteriological tests on the hydrazinopyrimidines are mentioned.

Eight of the possible eleven mono- and poly-chloropyrimidines have already been described and this paper records the synthesis of the remaining three, namely 4 : 5-dichloro-, 2 : 4 : 5-trichloro-, and 4 : 5 : 6-trichloro-pyrimidine. In addition, 5-bromo-4 : 6-dichloropyrimidine has been made and 5-bromo-4-chloropyrimidine (Cherbuliez and Stavritch, *Helv. Chim. Acta*, 1922, **5**, 273) prepared by a new route. Apparently, 5-bromopyrimidine (McOmie and White, *J.*, 1953, 3129) and 5-bromo-2 : 4-dichloropyrimidine (Wheeler and Bristol, *Amer. Chem. J.*, 1905, **32**, 437; Whittaker, *J.*, 1953, 1646) are the only other halogenopyrimidines previously known without other substituents present. The compounds now described were prepared in order to study their ultraviolet spectra (forthcoming publication; cf. Boarland and McOmie, *J.*, 1952, 3716, 3722) and their reactions with nucleophilic reagents.

4-Hydroxypyrimidine in glacial acetic acid, but not in aqueous solution, reacted with chlorine and with bromine to give 5-chloro- and 5-bromo-4-hydroxypyrimidine, respectively. The latter has already been prepared by the action of sodium hypobromite on *N*-methyleneasparagine followed by decarboxylation of the resulting 5-bromo-6-hydroxypyrimidine-4-carboxylic acid (Cherbuliez and Stavritch, *loc. cit.*). 5-Bromo-2-hydroxypyrimidine was obtained from 2-amino-5-bromopyrimidine by treatment with nitrous acid. 4 : 5-Dichloro- and 5-bromo-4-chloro-pyrimidine were prepared from the corresponding 4-hydroxy-compounds by reaction with phosphoryl chloride in presence of dimethylaniline (method of Baddiley and Topham, *J.*, 1944, 679).

Johnson (*Amer. Chem. J.*, 1908, **40**, 19) showed that the chlorination of uracil in aqueous suspension gave a mixture of 5 : 5-dichloro-5 : 6-dihydro-6-hydroxyuracil and 5-chlorouracil, but recorded no yields. By suitable choice of conditions, the former (70%) or the latter (55%) can be obtained as the main product, but the yields are not always reproducible. Conversion of 5-chlorouracil into 2 : 4 : 5-trichloropyrimidine was best effected by using a mixture of phosphoryl chloride and phosphorus pentachloride. An attempt to convert uracil directly into 2 : 4 : 5-trichloropyrimidine by heating it with a large excess of phosphorus pentachloride and phosphoryl chloride (2 : 1) gave only the known 2 : 4-dichloropyrimidine, whereas Childress and McKee (*J. Amer. Chem. Soc.*, 1950, **72**, 4271) obtained 2 : 4 : 5 : 6-tetrachloropyrimidine from barbituric acid under these conditions. Likewise, 5 : 5-dichloro-5 : 6-dihydro-6-hydroxyuracil could not be directly converted into the desired trichloro-compound.

Bromination of 4 : 6-dihydroxypyrimidine in warm water or, better, in acetic acid readily gave the 5-bromo-derivative, but chlorination proved surprisingly difficult. Chlorination at various temperatures in water, aqueous hydrochloric acid, or glacial acetic acid caused degradation of the pyrimidine, and ammonium chloride was the only isolable product. The required 5-chloro-compound was unexpectedly obtained when equimolecular amounts of chlorine and iodine (or more conveniently preformed iodine chloride) were used in warm glacial acetic acid. Iodine chloride normally behaves as an iodinating reagent and, for example, converts 4-amino- into 4-amino-5-iodo-pyrimidine under similar

* Part VII, *J.*, 1953, 4175.

conditions (D. J. Brown, *J. Soc. Chem. Ind.*, 1950, **69**, 353). The hydroxyl groups of the 5-bromo- and 5-chloro-4 : 6-dihydroxypyrimidines were replaced by chlorine by using phosphoryl chloride and dimethylaniline. Childress and McKee's method (*loc. cit.*) with 4 : 6-dihydroxypyrimidine gave only 4 : 6-dichloropyrimidine, instead of the desired 4 : 5 : 6-trichloro-compound.

The new halogeno-pyrimidines, like those previously described, all have a characteristic smell rather similar to that of acetamidine; they are lachrymatory, and must be handled with care. Some reactions of the compounds were studied; in all cases the halogen atom in position 5 was unreactive. Thus 4 : 5-dichloro- and 5-bromo-4-chloro-pyrimidine with ammonia gave the corresponding 4-amino-5-halogenopyrimidines which have also been prepared by Yanai (*J. Pharm. Soc. Japan*, 1942, **62**, 95) by direct halogenation of 4-aminopyrimidine. 4 : 5-Dichloropyrimidine with thiourea gave 5-chloro-4-mercaptopyrimidine (cf. Boarland and McOmie, *J.*, 1951, 1218); 2 : 4 : 5-trichloropyrimidine with sodium methoxide gave 5-chloro-2 : 4-dimethoxypyrimidine, and other reactions are given below.

Hydrazinopyrimidines.—In a previous paper (Boarland, McOmie, and Timms, *J.*, 1952, 4691) the results of bacteriological tests on some pyrimidines were recorded. 2-Hydrazino-4 : 6-dimethyl- and 2 : 4-dihydrazino-pyrimidine gave encouraging results and further hydrazino-compounds have been prepared and tested. 5-Chloro-, 5-bromo-, 5-phenyl-, 6-chloro-, and 2 : 5-dichloro-4-hydrazinopyrimidine and also 2-hydrazino-4-phenylpyrimidine were obtained from the corresponding chloropyrimidines by the action of hydrazine hydrate. Similarly, 2- and 4-hydrazinopyrimidine were prepared from the corresponding methoxypyrimidines. 2-Hydrazinopyrimidine has also been prepared from 2-chloropyrimidine (Sirakawa, Ban, and Yoneda, *J. Pharm. Soc. Japan*, 1953, **73**, 598).

The above-mentioned hydrazinopyrimidines (0·1—0·5% solutions in M/15 phosphate buffer of pH 7·38) were tested as before by the agar-cup diffusion method against *Staph. Mayo*, *Staph. H.*, *Str. viridans*, *Mycobact. butyricum* Sonne, *Proteus*, *B. coli*, *and B. pyocyaneus*. None of the compounds was active against *Str. viridans* or *B. pyocyaneus*, and 2-hydrazinopyrimidine and 2 : 5-dichloro-4-hydrazinopyrimidine were inactive against all the bacteria tested. Since the other hydrazino-compounds were inactive or at best less active than the two hydrazino-compounds previously tested, no details are given here.

Experimental

5-Chloro-4-hydroxypyrimidine.—Chlorine (1·5 g.) was bubbled into 4-hydroxypyrimidine (2·0 g.) in glacial acetic acid (15 ml.). After cooling, the fine, white hydrochloride (2·6 g.) was collected and dissolved in the minimum of cold water, and sodium hydrogen carbonate added until the solution became faintly alkaline. *5-Chloro-4-hydroxypyrimidine* (0·8 g.) slowly separated; recrystallised from water it formed prisms, m. p. 177—179° (Found: C, 36·7; H, 2·1; N, 21·3. $C_4H_3ON_2Cl$ requires C, 36·8; H, 2·3; N, 21·5%).

5-Bromo-4-hydroxypyrimidine.—Bromine (4·4 ml.) in glacial acetic acid was added gradually to 4-hydroxypyrimidine (8 g.) in acetic acid (200 ml.). After several hours, the product (17·2 g.) was recrystallised from ethanol giving *5-bromo-4-hydroxypyrimidine hydrobromide* as needles, m. p. 243—246° (decomp.) (Found: C, 19·6; H, 1·9; N, 10·9; Br, 61·3. $C_4H_3ON_2Br,HBr$ requires C, 18·8; H, 1·6; N, 10·9; Br, 62·5%). Recrystallisation of the hydrobromide from water gave 5-bromo-4-hydroxypyrimidine (6 g.) as leaflets (rapid cooling of a strong solution) or as needles (slow crystallisation from a dilute solution), m. p. 199—200° (Found: C, 27·1; H, 1·5; N, 15·9. Calc. for $C_4H_3ON_2Br$: C, 27·4; H, 1·7; N, 16·0%). Cherbuliez and Stavritch (*loc. cit.*) give m. p. 197°.

5-Bromo-2-hydroxypyrimidine.—2-Amino-5-bromopyrimidine (2 g.) was dissolved in hot concentrated sulphuric acid (2 ml.) and water (8 ml.), then the mixture was cooled rapidly. Aqueous sodium nitrite (1·5 g. in 10 ml.) was added with shaking during ½ hr., the temperature being kept at 5—10°. Next day, the solution was warmed to 75—85°, ammonia (*d* 0·88; 8 ml.) was added, and the solution was cooled. The product was dissolved in hot water (10 ml.) and acidified with glacial acetic acid (2 ml.). The precipitated *5-bromo-2-hydroxypyrimidine* was recrystallised from water, and then had m. p. 241—243° (0·5 g.) (Found: C, 27·8; H, 1·8; N, 15·9; Br, 45·3. $C_4H_3ON_2Br$ requires C, 27·4; H, 1·7; N, 16·0; Br, 45·7%).

5-Bromo-4-chloropyrimidine.—5-Bromo-4-hydroxypyrimidine (3 g.), phosphoryl chloride (22 ml.), and dimethylaniline (0·7 ml.) were heated for 3 hr., and then the mixture was cooled, poured on to ice, and extracted with ether (1 × 100, 6 × 15 ml.). The ethereal solution was shaken with saturated sodium hydrogen carbonate solution, dried, and then distilled. 5-Bromo-4-chloropyrimidine (1·6 g., 50%) was collected as a pale yellow oil, b. p. 87°/16 mm. (Found: C, 25·1; H, 1·1. Calc. for $C_4H_2N_2ClBr$: C, 24·8; H, 1·0%). Cherbuliez and Stavritch (*loc. cit.*) record b. p. 95·5°/26 mm.

4 : 5-*Dichloropyrimidine.*—5-Chloro-4-hydroxypyrimidine hydrochloride (18 g.), phosphoryl chloride (120 ml.), and dimethylaniline (2 ml.) were heated for 3 hr., then the product was isolated as in the preceding experiment. 4 : 5-*Dichloropyrimidine* (7·7 g.; 48%) was obtained as a pale yellow oil, b. p. 82°/34 mm. (Found: C, 32·4; H, 1·3. $C_4H_2N_2Cl_2$ requires C, 32·2; H, 1·3%). After a month the dichloro-compound had changed to a bright yellow solid.

5-Chlorouracil.—Chlorine was bubbled into a suspension of uracil (5·6 g.) in water (100 ml.) at 80—85° until practically all the solid had dissolved, and another solid was beginning to separate. The mixture was cooled and the 5-chlorouracil (4·0 g.) collected. After recrystallisation from water it had m. p. 314—318° (decomp.). Concentration of the mother liquor from the chlorination gave 5 : 5-dichloro-5 : 6-dihydro-6-hydroxyuracil (1·5 g.) as prisms, m. p. 212° (decomp.) after recrystallisation.

5 : 5-*Dichloro-5* : 6-*dihydro-6-hydroxyuracil.*—Chlorine was bubbled into a well-stirred suspension of uracil (5·0 g.) in water (40 ml.) on a boiling-water bath, until the solid had dissolved. On cooling, the 5 : 5-dichloro-compound separated as the monohydrate (6·9 g.). A portion of the material once crystallised from water had m. p. 216—218° (slight decomp.). Johnson (*loc. cit.*) recorded m. p. 212—215°.

2 : 4 : 5-*Trichloropyrimidine.*—5-Chlorouracil (10 g.), phosphoryl chloride (60 ml.), and phosphorus pentachloride (16 g.) were heated on a steam-bath for 1½ hr. then in an oil-bath (bath temp. 135—140°) for 24 hr. Distillation of the mixture gave 2 : 4 : 5-*trichloropyrimidine* (7·6 g.) as a lachrymatory oil, b. p. 73—74°/3 mm. (Found: C, 26·4; H, 0·4; N, 15·6. $C_4HN_2Cl_3$ requires C, 26·2; H, 0·5; N, 15·3%).

5-*Bromo-4* : 6-*dihydroxypyrimidine.*—Bromine (6 ml.) in acetic acid (60 ml.) was added gradually, with shaking, to a suspension of 4 : 6-dihydroxypyrimidine (12 g.) in acetic acid (60 ml.) at 70°. Next day, the crystalline hydrobromide was collected and recrystallised from water giving 5-*bromo-4* : 6-*dihydroxypyrimidine* (10·5 g.) as pale yellow microprisms, m. p. 263—264° (decomp.) (Found: C, 25·4; H, 1·6. $C_4H_3O_2N_2Br$ requires C, 25·1; H, 1·6%).

5-*Chloro-4* : 6-*dihydroxypyrimidine.*—Iodine chloride (16·3 g.) in acetic acid (100 ml.) was added to a suspension of 4 : 6-dihydroxypyrimidine (5·6 g.) in the same solvent (100 ml.). The mixture was heated on the steam-bath for 2½ hr. and then cooled. Crystallisation of the product from the minimum of hot water (*ca.* 500 ml.; charcoal) gave pale yellow 5-*chloro-4* : 6-*dihydroxypyrimidine* (3·8 g.), which decomposes without melting above about 230° (Found: C, 32·7; H, 1·9; N, 19·2. $C_4H_3O_2N_2Cl$ requires C, 32·7; H, 2·0; N, 19·1%).

5-*Bromo-4* : 6-*dichloropyrimidine.*—5-Bromo-4 : 6-dihydroxypyrimidine (2 g.), phosphoryl chloride (28 ml.), and dimethylaniline (1 ml.) were boiled for 3 hr. The product (1·1 g., 46%), isolated in the usual way, was purified by sublimation, giving the *bromo-compound* as plates, m. p. 75—76° (Found: C, 21·3; H, 0·4; N, 12·0. $C_4HN_2Cl_2Br$ requires C, 21·0; H, 0·4; N, 12·3%).

4 : 5 : 6-*Trichloropyrimidine.*—This was made from 5-chloro-4 : 6-dihydroxypyrimidine and purified as in the preceding experiment. The *trichloro-compound* (77%) formed needles, m. p. 49—51° (Found: C, 26·0; H, 0·4; N, 15·4. $C_4HN_2Cl_3$ requires C, 26·2; H, 0·5; N, 15·3%).

4-*Amino-5-bromopyrimidine.*—Ethanol was added to 5-bromo-4-chloropyrimidine (3 g.) and ammonia (*d* 0·88; 15 ml.) to give a homogeneous solution. After 48 hr., the solid was collected; evaporation of the mother liquor gave a further small crop. The total product was twice recrystallised from water giving 4-amino-5-bromopyrimidine (1·1 g., 41%) as yellowish needles, m. p. 208—210° (decomp.) (Found: C, 27·4; H, 2·2. Calc. for $C_4H_4N_3Br$: C, 27·6; H, 2·3%). Yanai (*loc. cit.*) gives m. p. 206—207°.

4-*Amino-5-chloropyrimidine.*—In the same way as that above, 4 : 5-dichloropyrimidine gave 4-amino-5-chloropyrimidine (65%) as leaflets, m. p. 192—194° (Found: C, 36·8; H, 2·9; N, 33·0. Calc. for $C_4H_4N_3Cl$: C, 37·1; H, 3·1; N, 32·5%). Yanai (*loc. cit.*) gives m. p. 191—192°.

5-*Chloro-4-mercaptopyrimidine.*—A solution of 4 : 5-dichloropyrimidine (0·6 g.) and thiourea (0·4 g.) in ethanol (25 ml.) was boiled for 1 hr., then concentrated to about 12 ml. and cooled.

The product was crystallised from ethanol giving the *mercapto-compound* (0·4 g., 68%) as pale greenish-yellow leaflets, m. p. 212° (slight decomp.) (Found: C, 32·7; H, 2·0. $C_4H_3N_3ClS$ requires C, 32·8; H, 2·1%).

5-Chloro-2 : 4-dimethoxypyrimidine.—2 : 4 : 5-Trichloropyrimidine (5·8 g.) was added very slowly and with thorough mixing to a solution of sodium methoxide [from sodium (5 g.) and methanol (100 ml.)]. After the initial strongly exothermic reaction, the mixture was boiled for 15 min., then cooled and filtered. The filtrate was saturated with dry carbon dioxide, and filtered again. Both residues were extracted with ether, and the extracts combined with the methanolic solution. Removal of the solvent and sublimation of the crystalline residue at 100°/11 mm. (bath temp.) gave *5-chloro-2 : 4-dimethoxypyrimidine* as needles (4 g., 74%), m. p. 72—73° (Found: C, 41·5; H, 4·1; N, 16·1. $C_6H_7O_2N_2Cl$ requires C, 41·3; H, 4·0; 16·1%.

2-Hydrazinopyrimidine.—2-Methoxypyrimidine (Boarland and McOmie, *J.*, 1952, 3716) (2·4 g.), hydrazine hydrate (100%; 1·6 ml.), and methanol (12 ml.) were heated for 2 hr. The methanol was removed by distillation, and after a few days the solid (0·5 g.) was collected. Recrystallisation from benzene–methanol gave 2-hydrazinopyrimidine as hygroscopic needles, m. p. 108—110° after thorough drying (Found: C, 44·0; H, 5·6; N, 50·6. Calc. for $C_4H_6N_4$: C, 43·6; H, 5·5; N, 50·9%). Sirakawa *et al.* (*loc. cit.*) record m. p. 86—88°.

4-Hydrazinopyrimidine.—This was prepared from 4-methoxypyrimidine (Brown and Short, *J.*, 1953, 331) as above. The *compound*, obtained in 55% yield, had m. p. 132—134° (decomp.) (Found: C, 43·8; H, 5·4; N, 50·4%).

Preparation of Hydrazino- from Chloro-pyrimidines. E.g., *5-Chloro-4-hydrazinopyrimidine.*—Hydrazine hydrate (100%; 4 ml.) was added gradually (vigorous reaction) to 4 : 5-dichloropyrimidine (3 g.) in ethanol (15 ml.). After a few hours, the solid *product* was collected and recrystallised from water, giving needles (1·1 g., 38%), m. p. 190—192° (Found: C, 33·2; H, 3·5; N, 38·9. $C_4H_5N_4Cl$ requires C, 33·2; H, 3·5; N, 38·8%).

Similarly 5-bromo-4-chloro- yielded *5-bromo-4-hydrazinopyrimidine* (48% yield), needles, m. p. 185—187° (decomp.) (Found: C, 25·7; H, 2·9. $C_4H_5N_4Br$ requires C, 25·4; H, 2·6%). 4-Chloro-5-phenyl- yielded slowly *4-hydrazino-5-phenyl-pyrimidine* (54% yield), needles, m. p. 140—141° (Found: C, 64·4; H, 5·7; N, 30·3. $C_{10}H_{10}N_4$ requires C, 64·5; H, 5·4; N, 30·1%). 4 : 6-Dichloro- yielded *6-chloro-4-hydrazino-pyrimidine* (34% yield), needles, m. p. 177° (decomp.) (Found: C, 33·1; H, 3·6; N, 38·8. $C_4H_5N_4Cl$ requires C, 33·2; H, 3·5; N, 38·8%). 2 : 4 : 5-Trichloro- yielded *2 : 5-dichloro-4-hydrazino-pyrimidine* (62% yield), needles, which gradually become yellow then black above 220° (Found: C, 26·8; H, 2·4; N, 31·0. $C_4H_4N_4Cl_2$ requires C, 26·8; H, 2·2; N, 31·3%). 2-Chloro-4-phenyl- gave *2-hydrazino-4-phenyl-pyrimidine* (25% yield), needles, m. p. 115° (Found: C, 64·7; H, 5·7; N, 30·3. $C_{10}H_{10}N_4$ requires C, 64·5; H, 5·4; N, 30·1%) [prepared by M. J. Abercrombie].

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Hydrogen Electrode Processes. Part I. Platinum–Hydrogen Electrodes.

By R. H. Cousens, D. J. G. Ives, and S. Swaroopa.

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The cathodic deposition of hydrogen from dilute acid solutions at bright platinum electrodes in very pure systems has been studied. Results have been obtained consistent with a cathodic component of the current limited by slow discharge, opposed by an anodic component due to ionisation. The behaviour of these electrodes, however, has been found to be critically dependent upon their surface state, for which no adequate means of control has yet been found. Two main kinds of variation in electrode properties have been observed and discussed. The properties of bright platinum electrodes in their resting state, and the behaviour of the cell formed from such an electrode combined with a platinised platinum electrode in a hydrogen-saturated acid solution have been investigated. The results lend support to a theory of the mechanism of the reversible hydrogen electrode previously proposed.

Hammett (*J. Amer. Chem. Soc.*, 1924, **46**, 7; *Trans. Faraday Soc.*, 1933, **29**, 770) studied the behaviour of bright platinum electrodes in hydrogen-saturated, aqueous hydrochloric acid. Electrode potentials, E, measured with respect to a reversible hydrogen electrode in the same solution, gave plots against current density, i, which passed through the origin with no change of sign of d^2E/di^2. With increasing cathodic polarisation, $dE/d\log i$ tended to a value of 0·118 v at 25° c for a number of electrodes of different activity. These characteristics are consistent with the behaviour of an electrode at which the net current is defined by a cathodic component limited by slow discharge and an anodic component due to ionisation. On this basis Hills and Ives (*J.*, 1951, 305) calculated the values of these discharge and ionisation components of the total current at Hammett's electrodes. The results supported the " differentiated site theory " of the hydrogen electrode mechanism developed by these authors from the well-known theory of Butler (*Proc. Roy. Soc.*, 1936, *A*, **157**, 423) on lines suggested by Audubert (*Discuss. Faraday Soc.*, 1947, **1**, 72).

Hammett's measurements, however, were not extended to cathodic potentials high enough to establish the Tafel slope, $b = 0{\cdot}118$ v, for the discharge process without ambiguity, and potential–current density curves of a different kind have been reported for platinum electrodes in a similar potential range (Volmer and Wick, *Z. physikal. Chem.*, 1935, *A*, **172**, 429; cf., however, Lorch, *Trans. Electrochem. Soc.*, 1936, **70**, 401; Dolin, Ershler, and Frumkin, *Acta Physicochim.*, 1940, **13**, 779). Although linear Tafel plots of slope near to 0·118 v have more recently been obtained with platinum electrodes of low activity (Kheifets and Polyakova, *Zhur. priklad. Khim.*, 1949, **22**, 801), the accepted view is that a slope of 0·029 v is typical of platinum, corresponding with rate limitation by slow recombination (Bockris, " Electrochemistry," Butterworths, 1954, p. 210). Change of mechanism at a given platinum electrode between one current density and another has been reported by Schuldiner (*J. Electrochem. Soc.*, 1952, **99**, 488) but, contrary to this author's statement, no sign of this can be found in Hammett's measurements. In general, it appears that platinum electrodes are capable of the most diverse behaviour under nominally similar conditions (cf. Parsons, *J. Chim. phys.*, 1952, **49**, 82); their great sensitivity to anodic activation and to the presence of impurities is well known. It is clear that the postulation of a single, exclusive mechanism for the hydrogen deposition reaction at platinum cannot be defended, and enquiry is needed into the conditions which promote one reaction mechanism or another. In particular, it seemed desirable to attempt a reproduction of the conditions which, in Hammett's work, led to a clear-cut reaction mechanism, ostensibly rate-limitation by slow discharge. This was the purpose of the present work, which, however, developed on somewhat unexpected lines.

In this work, bright platinum electrodes have been used as cathodes in the electrolysis of aqueous 0·1N-hydrochloric acid under the conditions of high purity now known to be essential for hydrogen overpotential measurements (Azzam, Bockris, Conway, and

Rosenberg, *Trans. Faraday Soc.*, 1950, **46**, 918). The method is fully described in the experimental section, but it may be mentioned that importance was attached to the following points in designing the electrolytic cell: (1) elimination of concentration polarisation and removal from the electrode surface of cathodically-generated hydrogen in the dissolved state by use of vigorous, non-turbulent stirring (Hammett, *loc. cit.*); (2) uniformity of current density over the whole electrode surface (Goodeve, *Discuss. Faraday Soc.*, 1947, **1**, 139); (3) exclusion of glass-to-metal seals in contact with solution (Garrett, Hogge, and Hukes, *Science*, 1940, **92**, 18); (4) provision for pre-treatment of electrodes by heating them in hydrogen and introducing them into the solution without exposure to air.

The first measurements to be reported were made with platinum electrodes which had been subjected to chemical cleaning processes (see Experimental section) but not to heat treatment in hydrogen. The dependence of electrode potential, referred to a hydrogen electrode in the same solution, upon current density was studied by the "rapid method," increments of current being made at fixed time intervals long enough for the potential at each current density to become sensibly constant. The reproducibility of the results was unsatisfactory and it became clear that an important variable defining electrode behaviour was neither properly understood nor controlled. This is believed to be the metallographic state of the bulk phase of the electrode and, in particular, the nature of its surface. In spite of this, results of the kind shown in Fig. 1 were obtained, but could not be depended upon in any given experiment. It is seen that they lead to Tafel plots with slopes varying somewhat on either side of 0·118 v, with deviations in the lower current density range of the kind expected from the effect of increasing ionisation with falling cathodic potential. In experiments in which nitrogen, instead of hydrogen, was passed through the electrolyte, these deviations were decreased, but not eliminated. It is clear that, under these conditions, the hydrogen atoms deposited by discharge of hydrogen ions partly combine to form molecular hydrogen and partly re-ionise. At the higher current densities, overpotentials were insensitive to change of gas, confirming that the back-reaction, or ionisation, was suppressed at sufficiently high cathodic polarisations. This is consistent with the repression of deuterium exchange between gas and solution phases at platinum by cathodic polarisation, whilst the concomitant acceleration of para-hydrogen conversion indicates increased production of hydrogen atoms and maintenance of the atomisation–recombination equilibrium (Calvin, *Trans. Faraday Soc.*, 1936, **32**, 1428).

These results, obtained with electrodes of differing activity, support the view that under suitable, but ill-defined, conditions the hydrogen deposition reaction at platinum follows a Tafel law consistent with rate-limitation by slow discharge, and therefore satisfy, with some reservation, the original objective of the work.

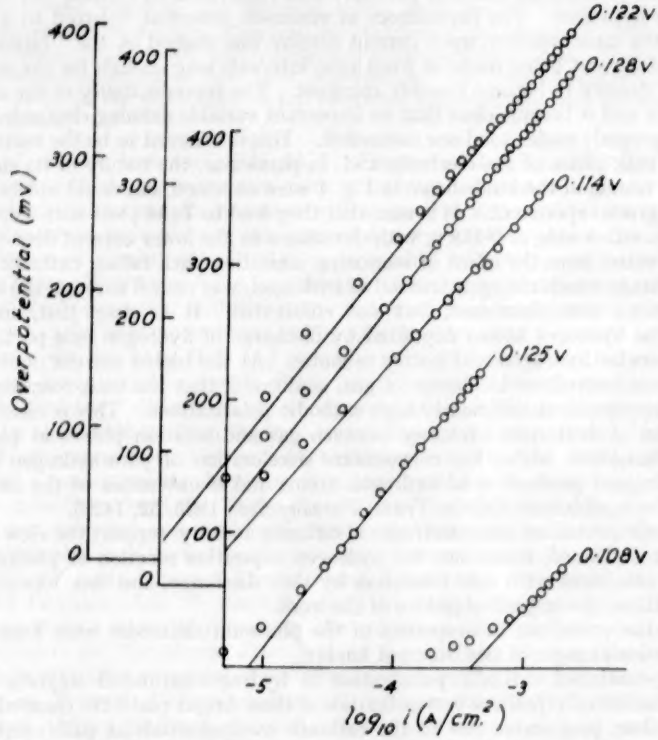
Some of the variations in properties of the platinum electrodes were found to result from progressive changes of two different kinds:

(1) Long-continued cathodic polarisation in hydrogen-saturated solution caused an increase in the initially positive rest-potentials of these bright platinum electrodes. There was also a slow, progressive rise in the cathodic overpotentials at each current density (cf. Butler and Armstrong, *J.*, 1934, 746) and an increase in the slopes of the linear sections of the Tafel plots (cf. Bowden, *Proc. Roy. Soc.*, 1929, *A*, **126**, 107). This kind of behaviour has been attributed to poisoning. It was, however, observed that this change in the electrode system was arrested and reversed by allowing the electrode to rest whilst sweeping out the solution with nitrogen. This suggests that the "poisoning," or deactivation, may have been due to progressive absorption of hydrogen by the electrode, and its reversal to slow desorption from the metal in a system rigorously freed from hydrogen.

(2) The repeated use of an electrode in successively assembled cells, with intervening exposure to air and cleaning agents, caused a fall of positive rest-potential to zero, a decrease of cathodic overpotential at a given current density, and a rapid fall of Tafel slope. Consecutive values of this slope in one sequence of experiments were: 0·120, 0·096, 0·083, and 0·055 v. It is evident that this kind of change is associated with progressive activation of the electrode, no doubt because of its alternate exposure to oxidising and reducing conditions.

Loss of activity on prolonged cathodic polarisation, attributable to "hydrogen poisoning," has been observed before (Baars, *Ber. Ges. Beförd. Naturw. Marburg*, 1928, **63**, 213; Butler and Armstrong, *loc. cit.*; Masing and Laue, *Z. phys. Chem.*, 1936, **178**, *A*, 1), and it is of interest that Bodenstein (*Annalen*, 1924, **440**, 177) found that saturation with hydrogen reduced the catalytic activity of palladium. It is of particular interest that the Tafel slope decreases with increasing electrode activity. Knorr and Schwartz (*Z. phys. Chem.*, 1936, **176**, *A*, 161) found this to be the case for palladium, measuring catalytic activity unequivocally in terms of the rate at which a given electrode would take up hydrogen from the gas phase. The situation appears to arise that the more active an electrode in catalysing recombination, the more consistent is its Tafel slope with rate

FIG. 1.



limitation by recombination; special pleading therefore seems to be necessary to maintain the view that recombination is rate-limiting at platinum or palladium. It seems probable that low Tafel slopes more frequently arise in the manner indicated by Kandler, Knorr, and Schwitzer (*ibid.*, 1937, **180**, *A*, 281).

An attempt was made to obviate these uncontrolled variations in electrode properties by heat-treatment of an electrode in hydrogen. This was done by withdrawing the electrode from the solution into a silica furnace tube which formed an integral part of the electrolytic cell, in which the electrode was heated in hydrogen, cooled, and restored to the same solution. Treatment of this kind was ineffective in bringing the electrode to a standard state; on the contrary, the behaviour afterwards was characterised by curved Tafel plots reaching very high slopes at the higher current densities. This has been ascribed to a highly inhomogeneous electrode surface which changes rapidly in properties as a function of current density (Busing and Kauzmann, *J. Chem. Phys.*, 1952, **20**, 1129).

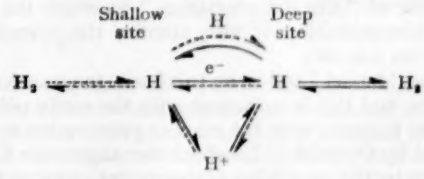
Further work designed to control electrode state and to trace its effect on electrochemical behaviour was carried out with gold, under the supposition that this metal might show less extreme variations of properties than platinum, and is described in the following paper. One aspect of this problem, however, may be discussed immediately.

The persistent positive rest-potentials often shown by bright platinum electrodes in hydrogen-saturated, acid solutions have long been known (Plzák, *Z. anorg. Chem.*, 1902, **32**, 385) and have been attributed to poisons in solution, removable by prolonged contact with platinised platinum (Aten and Zieren, *Rec. Trav. chim.*, 1929, **48**, 944). It is difficult to explain the persistence of a potential difference for months between bright and platinised platinum, in hydrogen-saturated hydrochloric acid, in a closed system in this way, for such a system should be " self-cleaning " (Beans and Hammett, *J. Amer. Chem. Soc.*, 1925, **47**, 1215). In any case, the phenomenon is of interest and possible value in the elucidation of the hydrogen electrode mechanism, and some new experiments bearing upon it have been made.

Two platinised platinum, one bright platinum, and one gold electrode were enclosed, together with 0·1N-hydrochloric acid and hydrogen, in a totally-sealed, vacuum-tight cell, every effort being made to secure high purity. The platinised platinum electrodes were used as reference electrodes. The initial rest-potentials of the bright platinum and gold electrodes were +340 and +420 mv and were persistently recorded after the disturbing effects of interconnection of the electrodes, gentle cathodisation or anodisation, or heating to 90° had died away. Connection of either of these electrodes to one of the platinised electrodes showed, on a microammeter, an inital current flow of about 10 μA, falling rapidly to a steady value of about 0·5 μA which persisted indefinitely, but was greatly increased by shaking the cell. With rise of temperature, the potential of the bright platinum electrode fell to zero at 70°; that of the gold electrode decreased steadily by about 2 mv per degree, both these changes being reversible. After three weeks on open circuit, *both* rest-potentials had fallen by 80 mv, and after two months by about 330 mv. The identical decline in the apparent positive potentials of the dissimilar electrodes indicated that the change had really taken place in the reference electrodes by a process of slow deactivation.

These results may be discussed in relation with the " differentiated site theory " of the hydrogen electrode (Hills and Ives, *loc. cit.*). According to this theory a satisfactory, reversible hydrogen electrode must have surface sites of widely varying adsorption energy, for only in this way can an exchange current of adequate magnitude be attained. Discharge of hydrogen ions occurs preferentially at the " deeper " adsorption sites; ionisation of hydrogen atoms occurs more easily from " shallower " sites, sufficiently free migration of adsorbed atoms over the surface providing the necessary redistribution. This reaction scheme is represented formally in Fig. 2, where, for simplicity, only two kinds of site are shown.

FIG. 2.



Heavy arrows show the predominant directions of the various partial processes. It will be noted that the deep sites are cathodic and the shallow sites anodic, and that electrons flow within the metal phase from one to the other in a manner precisely analogous to the flow of current between local elements discussed in corrosion theory. If the two kinds of site are close together, the whole reaction scheme is mobile and the exchange current considerable; if they are far apart, the migration of adsorbed hydrogen atoms will be hindered. If, in the limit, the two kinds of site are situated on separate pieces of platinum, the migration of hydrogen atoms from one to the other becomes impossible and the general equilibrium scheme of Fig. 2 must be disturbed. The cell formed from bright and platinised

platinum electrodes acts as a model in which the main kinds of site are completely separated. Its behaviour may be discussed on the assumption that the general equilibrium scheme will always be established as far as conditions permit.

Although the bright electrode carries mainly shallow adsorption sites, hydrogen-ion discharge can occur at this electrode with some facility, if less readily than at the platinised electrode. This has been strikingly shown by examination of the behaviour of a bright platinum electrode in an electrolyte of constant-boiling hydrochloric acid vigorously swept out with nitrogen. The following table records cathodic current densities and corresponding potentials measured with respect to a platinised platinum electrode in equilibrium with the same solution and with hydrogen gas at 1 atm. pressure.

E (mv)	10	20	50	100	200	500	565
i (μA/cm.^{2})	36	22	2·8	1·2	0·8	0·3	0

Ionisation of hydrogen atoms, on the other hand, is believed to take place more easily at a bright platinum surface than at a platinised one. But in the " model " cell under discussion, the supply of hydrogen atoms to the bright electrode is restricted, for the bright platinum is not a very active catalyst for the atomisation of molecular hydrogen (Butler and Armstrong, *J.*, 1934, 734). The electrode thus acquires little atomic hydrogen from this source and none by any migration process. In these circumstances the main source of hydrogen atoms at the bright electrode is the discharge process. Thus, although intrinsically easier, ionisation at this electrode must wait upon discharge, and the electrode will assume such a positive potential as to bring the rates of these opposing processes to equality. This is considered to be the source of the positive rest-potential of the bright platinum electrode, which therefore carries a surface concentration of hydrogen atoms not in equilibrium with the gas phase (cf. Butler and Armstrong, *J.*, 1934, 732). This is known to be the case (Slygin and Frumkin, *Acta Physicochim.*, 1935, **3**, 791; Ershler, *ibid.*, 1937, **7**, 327; Pearson and Butler, *Trans. Faraday Soc.*, 1938, **34**, 1163; Hickling, *ibid.*, 1945, **41**, 333; Wicke and Weblus, *Z. Elektrochem.*, 1952, **56**, 169). The effect of increasing temperature is consistent with this view, for as the hindered atomisation process occurs with increasing facility, the electrode eventually becomes reversible and its rest-potential falls to zero. Insofar as poisons promote these positive rest-potentials, it may be suggested that their poisoning action is exerted principally upon the atomisation process (cf. Aten and Zieren; Volmer and Wick; *locc. cit.*).

This interpretation carries implications which will not be discussed at present, but it must be further examined in relation to the behaviour of the " model " cell. When the external circuit is closed, electrons flow from the platinised electrode to the bright electrode, increasing the rates of discharge and of ionisation, respectively, at these electrodes. The two, connected directly together, operate as a reversible hydrogen electrode at the proper equilibrium potential (Beans and Hammett, *loc. cit.*). This multiple hydrogen electrode offers an extreme example of " site differentiation," in which the normally unobserved local currents become demonstrable; it also clarifies the operation of the " catalyst electrode " of Hills and Ives (*loc. cit.*).

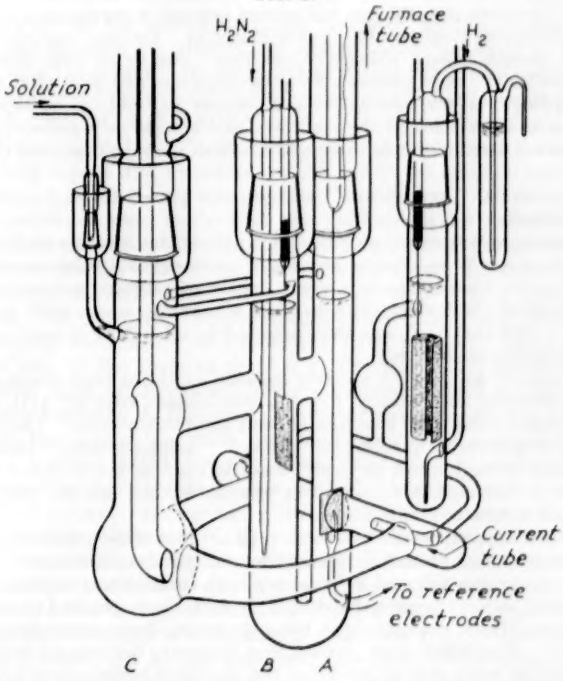
The cell reaction of the " model " cell is, on this basis, the transfer of hydrogen gas from one electrode to the other, and this is consistent with the ready polarisation which occurs when current is allowed to pass and with the relief of polarisation by shaking. This, however, is the example used by Ostwald (" Lehrbuch der allgemeine Chemie," 1903, II, 896) of a cell reaction forbidden by the second law of thermodynamics, so that some other change must be involved. This is found by consideration of the platinum electrodes. It is known that hydrogen electrodes are subject to fatigue and become inactive with increasing age at a rate which increases with the removal of the last traces of oxygen from the solution. Hammett and Lorch (*J. Amer. Chem. Soc.*, 1933, **55**, 70) have found that platinum black slowly loses activity when it is kept in hydrogen, and attribute this to the sintering of active points at which the highly exothermic recombination of hydrogen atoms continually occurs. There can be no doubt that electrolytically deposited platinum black is higher in energy content than the same weight of massive platinum, and that the dissipation of this excess of energy is a natural process attended by a decrease in free energy. Since, in

the cell under discussion, this cannot occur by processes of anodic dissolution and cathodic re-deposition of the metal itself, an alternative mechanism operates in which the hydrogen acts as the intermediary. Calculations in orders of magnitude of the probable energy terms involved show this explanation to be feasible. The total cell reaction does not therefore infringe the second law, and the discussion based upon the behaviour of this cell stands.

Experimental

Electrolytic Cell.—The electrolytic cell is illustrated in Fig. 3. The rectangular test electrode of " thermopure " platinum foil, 0·05 mm. thick and 5·2 cm.^{2} in apparent surface area, was welded to a suspension wire of the same metal. It was accurately located in the cathode compartment, *A*, by internal glass seatings so arranged as to obscure the working surfaces of the electrode as little as possible. An all-glass centrifugal stirrer, driven by glass shafting running

Fig. 3.



in unlubricated, precision-ground, water-cooled glass bearings, provided a rapid flow of solution, normal to each electrode face, the solution returning to the stirring chamber, *C*, *via* alternative upper and lower paths. Rate of stirring, uncritical above a certain limit, was standardised by means of a Weston tachometer. Symmetrical design of the cell ensured the even distribution of current over both electrode faces; two " current tubes," equally spaced from the electrode on either side, communicated with an ancillary electrode vessel containing a very large working hydrogen electrode, at which the anodic reaction was hydrogen ionisation. Luggin capillaries approached the two sides of the electrode and communicated with a separate compartment containing duplicate reference hydrogen electrodes. A fifth electrode was situated in the " solution return " compartment, *B*, and consisted in the present experiments of a large platinised platinum electrode for purposes of final de-oxygenation and purification of the solution (Aten and Zieren, *loc. cit.*).

A " Vitreosil " furnace tube was fitted above compartment *A*. The test electrode could be raised into, or lowered from, this tube by means of a long, cylindrical ground joint, the inner

member of which carried the supporting wire for the electrode. Connection to the electrode was made by means of a coil of fine platinum wire, welded to the upper end of the supporting wire and issuing from the apparatus through a gas outlet bubbler at the top of the furnace tube. All the head fittings to the cell were attached by solution-sealed ground joints. A pressure of hydrogen, or nitrogen, in excess of atmospheric pressure was always maintained in the cell and could be sustained without passing gas for a prolonged period. Purified gases were supplied to the main cell by a bubbler entering compartment *B*.

Measuring Instruments.—Current, stabilised by variable series resistances (10^3 to 5×10^6 ohms), was measured by means of a multi-range microammeter, calibrated in terms of the *iR* drop across Sullivan standard resistors. E.M.F. measurements were made with a Tinsley 4025 potentiometer in the usual way. Attention was paid to screening and to insulation; Polythene and Silicone products were used where appropriate.

Materials.—Hydrogen. Commercial "oxygen-free" hydrogen used in some of the experiments was later replaced by hydrogen purified by active carbon at a pressure of 100—140 atm. and −196°. This gas was supplied by the British Oxygen Co., Ltd., and was stated to be of 99·998% purity. In either case the gas was passed through a purification train containing in its final form the following components: Baker Platinum "De-oxo" cartridge, non-absorbent cotton-wool filter, potash pellets, reduced "Specpure" copper at 500—550°, trap at −80°, platinised asbestos at 300°, traps packed with glass fragments and long glass spirals at −183°. Distribution of hydrogen to the various cell components was effected by tap systems, grease-lubricated, separated from the cell by the traps and spirals at liquid-oxygen temperature. No effect was observed attributable to change in source of hydrogen supplied to this purification train.

Nitrogen. Commercial "oxygen-free" nitrogen was passed through a similar purification train, suitably modified.

Water. Conductance water was prepared in a still of the Stuart and Wormwell type (*J.*, 1930, 85), in which steam from alkaline potassium permanganate solution was scrubbed with dilute phosphoric acid, admixed with a rapid stream of purified, oxygen-free nitrogen, and condensed in a Vitreosil condenser. The distillate was run to waste until its conductance fell to less than $0{\cdot}08 \times 10^{-6}$ ohm^{-1}; it was then collected in a 5-l. flask in which an atmosphere of pure nitrogen was always maintained.

Hydrochloric acid. "AnalaR" potassium chloride was freed from traces of other halogens by the method of Pinching and Bates (*J. Res. Nat. Bur. Stand.*, 1946, **37**, 311), and twice crystallised from conductance water with rejection of head and tail fractions. The product was dried at 150° and used to generate, by action of "AnalaR" sulphuric acid, hydrogen chloride gas, which, after passing through traps at −80°, was absorbed in conductance water. The concentrated solution so obtained was distilled as constant-boiling mixture and stored in a silica vessel under an atmosphere of pure nitrogen.

Procedure.—Glass apparatus was cleaned for 12 hr. in freshly prepared chromic–sulphuric acid, washed throughly, and soaked for several hours in conductance water. Further washing with conductance water was followed by steaming from conductance water and drying at 100°. The cell was mounted in the thermostat bath (25° ± 0·01°) and attached to the gas supply lines by glass-blowing operations, the apparatus being protected from contamination by means of a liquid-oxygen trap. Electrodes were cleaned first in warm, moderately concentrated hydrochloric acid, washed in water and suspended in the vapour of boiling nitric acid (*d* 1·50). They were then washed again, steamed from conductance water, and dried at 150° before being mounted in the cell. Working, reference, and deoxygenating electrodes were platinised by the method of Hills and Ives (*loc. cit.*) from a solution containing no lead.

After completion of the cell assembly, nitrogen was passed through the various cell compartments for 24 hr., followed by similar passage of hydrogen for at least 24 hr. The solution, prepared from constant-boiling hydrochloric acid and conductance water, without exposure to air at any stage, and through which hydrogen had been passed for 48 hr., was then introduced into the cell by pressure of hydrogen. The solution delivery tube was then sealed. Hydrogen was passed through the solution in the cell, circulated by the stirrer, for some hours before the start of electrical measurements.

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Hydrogen Electrode Processes. Part II. Gold–Hydrogen Electrodes.*

By D. J. G. Ives and S. Swaroopa.

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The electrodeposition of hydrogen from dilute acid solutions at gold electrodes has been studied, with results which show similarities with, and some differences from, this reaction occurring at platinum. The nature of the gold electrode, however, has been found to be radically changed by thermal pretreatment in hydrogen, the behaviour then corresponding with that of a "non-equilibrium atomic hydrogen electrode." The phenomena observed are discussed in terms of a postulated penetration of the metal phase by hydrogen atoms and in relation to mechanisms of desorption of hydrogen atoms from the gold–solution interface.

The work described in the preceding paper indicated that the characteristics of the hydrogen electrode reaction are strongly dependent upon the state of the metal surface upon which the reaction occurs. It was therefore thought that gold could be brought more easily to a standard state than could platinum, and would therefore be more suitable as a substrate for purposes of studying the mechanism of this reaction. Work with gold electrodes was accordingly started, with results of so unexpected and novel a nature as to merit a preliminary report and discussion. This forms the subject matter of the present paper.

The first experiments were made with fine gold electrodes under conditions exactly similar to those used previously for platinum, with no thermal pretreatment in hydrogen, and gave analogous results. Reproducibility was poor, but the following general statements can be made. Rest-potentials, measured with respect to a hydrogen electrode in the same solution, were positive. Measurements of the dependence of electrode potential upon current density were made which yielded Tafel plots the linear sections of which varied on either side of the slope of 0·118 v at 25° and which showed deviations from linearity consistent with an ionisation process increasing with falling current density. There was the same tendency for the Tafel slope to increase as a result of prolonged cathodic polarisation as in the case of platinum, and the same partial reversal of this change by sweeping out the solution with nitrogen. Two Tafel plots of measurements on a gold electrode, conducted by the "discontinuous method," recommended particularly for gold by Hickling and Salt (*Trans. Faraday Soc.*, 1940, **36**, 1226), are shown in Fig. 1 for hydrogen- and nitrogen-saturated solutions. It is noteworthy that polarisation curves for gold electrodes obtained in solutions swept out with hydrogen and nitrogen, respectively, do not appear to approach coincidence at the higher cathodic potentials, as is the case with platinum electrodes. The electromotive sensitivity of a metal to gaseous hydrogen requires a certain facility for atomisation of hydrogen molecules and for ionisation of hydrogen atoms. The loss of sensitivity by platinum with increasing cathodic polarisation can only be due to the suppression of the ionisation process, since it is unlikely that atomisation is ever potential-dependent (cf. Horiuti and Okamoto, *ibid.*, 1936, **32**, 1492; Calvin, *ibid.*, p. 1428). The sensitivity retained by gold under similar conditions shows that this metal is able, if less efficiently than platinum, to catalyse the atomisation of molecular hydrogen and has perhaps a greater facility than platinum in ionising hydrogen atoms. This is perhaps why no depolarisation due to adsorbed hydrogen is normally observed at gold (Hickling, *ibid.*, 1946, **42**, 518). It will become clear, however, that general statements about the properties of a metal may be falsified by the great variations in these properties which may occur as a function of the thermal and mechanical history of the metal. For the particular electrodes under discussion, however, it may be stated that all the "partial processes" of the hydrogen electrode equilibrium can take place at gold, but the balance between them is different from that which applies at platinum.

Heat treatment of a gold electrode in hydrogen gave rise to entirely new properties.

* Part I, preceding paper.

This operation involved withdrawal of the electrode from the solution into a furnace tube attached to the cell and its restoration to the same solution, after heating and cooling, without exposure to air at any stage. The electrode was, typically, maintained at 750—800° for 6 hr., then at 500° for 17 hr., and finally subjected to slow cooling, in a stream of hydrogen passing up the furnace tube from the cell. This annealing process was designed to bring the electrode to a reproducible standard state. After this treatment, a representative electrode showed a reproducible rest-potential of +400 mv. A " polarisation run " by the usual rapid method gave a very abnormal Tafel plot of the kind shown in Fig. 2, which includes for comparison another plot judged to be normal for untreated, rather active gold. Overpotentials were greater than those recorded for the same electrode in the same solution before annealing (*e.g.*, 550 and 270 mv respectively at 2 mA/cm.²) and greater than any overpotentials previously recorded for gold. Rest-potentials and overpotentials were almost completely insensitive to replacement of hydrogen by nitrogen in the cell, in remarkable contrast to the previous behaviour. It may be noted that the abnormal curve in Fig. 2 resembles those reported by Hitzler and

FIG. 1.

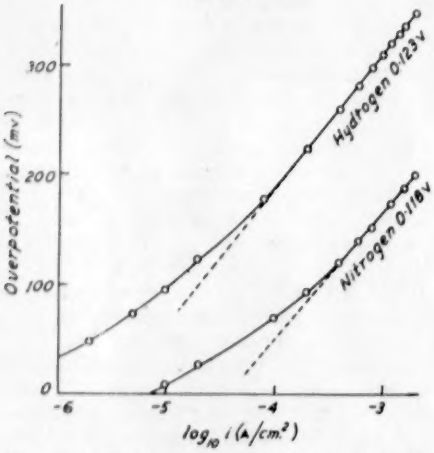
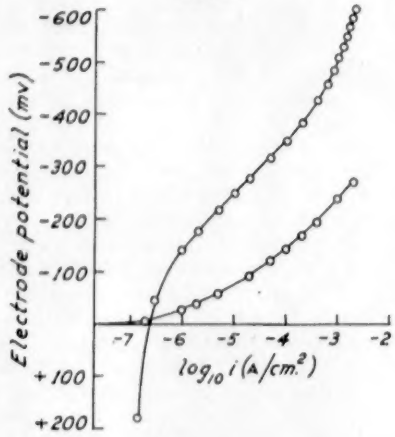


FIG. 2.



Knorr (*Z. Elektrochem.*, 1949, **53**, 228) for catalytically inactive metals at which, according to these authors, recombination of hydrogen atoms occurs slowly, leading to the establishment at low current densities of an adsorption layer, offering hindrance to the discharge process.

It became evident, however, that the annealing process had caused even more radical changes in the properties of the gold, calling for thorough and detailed investigation. Circumstances do not allow this to be pursued immediately; the present report will therefore be confined to a description of the more outstanding phenomena and their provisional interpretation.

For the unannealed electrodes, a rapid growth of overpotential occurred from the instant that a constant current density was established, leading to a steady value showing no further significant change in a period of one hour. The annealed electrodes showed a complex growth of overpotential, which, without detailed analysis, may be described as follows. An initial period of rapid growth passed smoothly into an indefinitely prolonged period of slow growth. Constancy of overpotential was not attained in 6 hr., the longest time for which polarisation was continued. This behaviour must be associated with a continuous and progressive change in the state of the electrode concerned. This is supported by the effect of a sudden reduction in the polarising current density; an immediate fall of overpotential was instantly followed by a period of growth faster than before (cf. Busing and Kauzmann, *J. Chem. Phys.*, 1952, **20**, 1129).

The properties of an annealed gold electrode after prolonged cathodic polarisation were very abnormal. On breaking the polarising circuit, the negative potential of the electrode fell rapidly, linearly with log time, to a value of about −150 to −200 mv with respect to a hydrogen electrode in the same solution. From this point, the potential decayed rapidly at first, then more slowly, passing through zero and eventually returning to its original resting value of +400 mv. These changes were slow enough to allow brief investigations

FIG. 3.

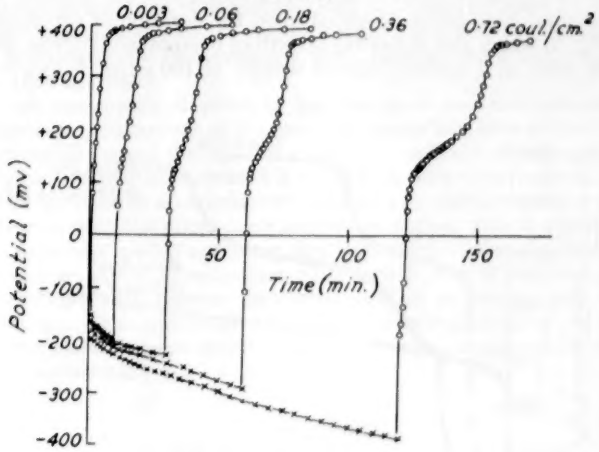
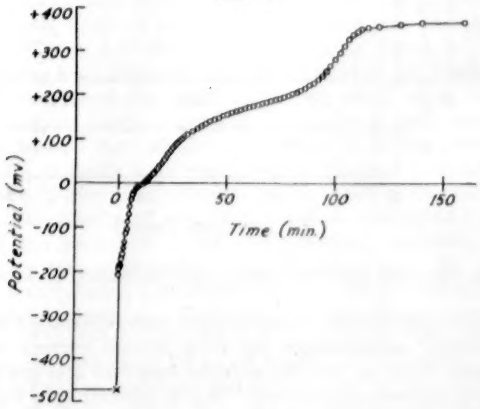


FIG. 4.



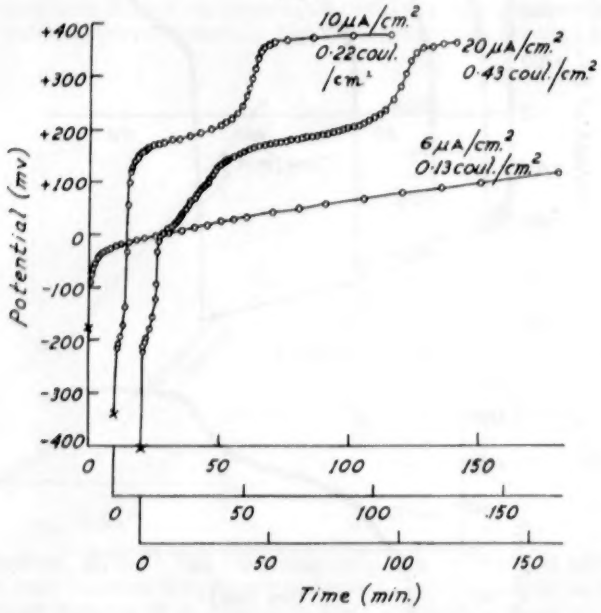
of the properties of the electrode both before and after its potential crossed the reversible hydrogen potential. This was done by connecting the electrode to the hydrogen electrode *via* a microammeter. Whilst the electrode potential was still negative, this connection caused a current, initially of a few microamperes, to flow anodically at the gold electrode. This current slowly decayed, but was temporarily enhanced by stirring. On disconnection, partial recovery of the negative potential took place before resumption of the original slow decay. When the electrode potential had passed spontaneously to positive values, the same operation caused cathodic current to flow at the gold electrode, enhanced by stirring and persisting for the longest period studied, 16 hr. On disconnection, the potential changed immediately in the direction of the final rest-potential, +400 mv. These

experiments leave no doubt that the potentials through which the electrode passes after cathodic treatment are well-defined potentials, decisively determined by the state of the electrode at each instant. The state of the electrode at any time is, in turn, a function of the stage reached in a slow reaction at the electrode-solution interface, leading finally to a steady resting state.

The course of the slow potential changes after cessation of cathodic polarisation attracted interest, and the following facts have been established :

(1) For a given constant current density of cathodisation, the course of the subsequent open-circuit potential–time curve depended upon the duration of cathodisation. This is illustrated in Fig. 3, which also shows the growth of overpotential during periods of ½, 10, 30, 60, and 120 mins. at a uniform current density of 100 μA/cm.², and in Fig. 4, which

FIG. 5.



records the change in potential with time after a cathodisation of 6 hr. at the same current density.

(2) The form of the open-circuit potential–time curve depended strongly upon current density in the preceding cathodisation up to a certain current density. Above this critical current density, however, this dependence vanished and the curve then became a function of the time of cathodisation alone. This is illustrated in Fig. 5, which shows the changes of potential with time after 6-hr. cathodisations at current densities of 6, 10, and 20 μA/cm.². It is seen that the last of these curves is nearly identical with that of Fig. 4, relating to 100 μA/cm.². This effect is believed to be associated with the attainment during the preceding cathodisation of an electrode potential exceeding about −300 mv. If this critical value was exceeded, the subsequent potential-decay curve assumed sensibly the same inflected form.

(3) At no stage of overpotential growth and decay did any annealed gold electrode show any perceptible effect when hydrogen passing through the cell was replaced by nitrogen; it was as if the annealing process had, in some respects, caused the electrode to become isolated from its surroundings.

(4) The observed effects depended upon electrode material in the following way.

Results obtained with a given electrode of fine gold were reproducible with some accuracy. Other electrodes prepared from the same sample of fine gold gave results in close correspondence. A second sample of fine gold, of independent history, furnished electrodes which gave similar, but not identical results. Finally, an electrode of spectroscopically pure gold showed considerable disparity, but in the sense of enhanced abnormality, with even higher overpotentials subject to more protracted decay of the same inflected type.

Two further observations on experimental aspects of this work must be made. During prolonged cathodic polarisation of unannealed gold electrodes, adherent bubbles of hydrogen were formed at localised places on the electrode surface and were not dislodged by vigorous stirring. It is thought to be significant that bubbles were not formed on any of the electrodes after annealing.

Since interest was mainly devoted to the change in electrode properties caused by annealing in hydrogen, all but one of the annealing operations were carried out in a stream of hydrogen that had passed through the electrolytic cell already charged with solution, in which the electrode had already been given preliminary examination. The annealing process therefore occurred in an atmosphere of hydrogen containing water vapour. There is reason to believe that the presence of this water vapour was of significance, for, in a single case, an otherwise similar annealing operation conducted in dry hydrogen had little effect. A systematic study of annealing conditions is clearly required. The range of potentially significant experimental conditions studied in the present work has been unavoidably limited. The invariable appearance of new phenomena as a result of the same specified thermal treatment of the electrodes, however, suggests that these phenomena are of fundamental interest.

Discussion

Positive rest-potentials, and high overpotentials, increasing with time during cathodic polarisation at constant current density, and subject to slow and inflected decay on open circuit after polarisation, have all been observed before and have been attributed to the presence of poisons (Volmer and Wick, *Z. phys. Chem.*, 1935, **172**, *A*, 429; Bockris and Conway, *Trans. Faraday Soc.*, 1949, **45**, 989; Bowden, *ibid.*, 1927, **23**, 571). The technique of the present work minimised the incidence of poisoning, which was not evident in the behaviour of the electrodes before annealing. The effects were, moreover, evoked by the annealing process alone and were of a magnitude out of all proportion to any conceivable poisoning effect. It is probable, however, that the thermal treatment in hydrogen had a similar effect to that of poisons in destroying catalytically active centres on the surface of the electrode. That this treatment radically altered the surface of the metal was confirmed by examination of the electrode under the reflecting polarising microscope. Before annealing, the surface was apparently structureless, except for what appeared to be mechanical scratches and scores, but afterwards it showed a definite crystalline structure with well-marked grain boundaries. It is probable that the presence of hydrogen exerted an additional effect. Thus, Hammett and Lorch (*J. Amer. Chem. Soc.*, 1933, **55**, 70) have shown that platinum is deactivated by gentle heating in hydrogen. This they attributed to the "burning out" of active centres by the great energy effect of the reaction $H_2 \rightleftharpoons 2H$ initially established at these centres. A similar mechanism may operate during the annealing of the gold electrodes in hydrogen, with the additional possibility of the co-operation of the reaction $H_2O \rightleftharpoons H_2 + \frac{1}{2}O_2$, due to the water vapour present under the conditions of our experiments, in the de-activating process. It is known that heating in moist hydrogen exerts a passivating effect on platinum (Ershler, Deborin, and Frumkin, *Acta Physicochim.*, 1938, **8**, 565).

The possibility that this treatment might lead to the firm adsorption of OH radicals on the gold has been considered. It is known, however, that oxygen or oxide films on gold exert a depolarising action at quite high positive potentials (Armstrong, Himsworth, and Butler, *Proc. Roy. Soc.*, 1933, *A*, **143**, 89; Deborin and Ershler, *Acta Physicochim.*, 1940, **13**, 347; Hickling, *Trans. Faraday Soc.*, 1946, **42**, 518). Such films could hardly resist

prolonged cathodic polarisation so as to effect a permanent change in electrode properties. Simultaneous adsorption of H and OH to any significant extent would be highly metastable (cf. Bennewitz and Schieferdecker, *Z. phys. Chem.*, 1931, **157**, *A*, 32). It is therefore thought that this treatment undoubtedly altered the properties of the gold itself, for it is known that this metal is susceptible to significant structural changes at temperatures as low as 450° (Chung Fu Ying and Farnsworth, *Phys. Rev.*, 1952, **85**, 485).

Whatever detailed interpretation may be found for the processes occurring during annealing, there is no doubt of their effects upon the gold electrodes in causing profound deactivation. Beforehand, their behaviour was consistent with rate-limitation of cathodic hydrogen deposition by slow discharge. This implied that hydrogen-atom recombination occurred without significant hindrance and this is confirmed by the sensitivity of the electrodes to gaseous hydrogen. This sensitivity must be due to catalysis of atomisation which must be associated with catalysis of recombination. Afterwards, the complete insensitivity of the electrodes to gaseous hydrogen, and their ability to sustain very high positive rest-potentials, indicate clearly that catalytic activity had been lost. In this state of the electrodes, cathodic hydrogen evolution no longer followed any clear-cut kinetic law. It is obvious that the overpotentials, slow in build-up and decay, were composite, being partly due to the hindrance of a reaction step and partly due to the accumulation of electromotively active cathodic products. There is a close analogy with the case of palladium, at which the hydrogen overpotential is the sum of two contributions (Hitzler, Knorr, and Mertens, *Z. Elektrochem.*, 1949, **53**, 228), one of which is transferable through a palladium membrane and the other not (Frumkin and Aladjalova, *Acta Physicochim.*, 1944, **19**, 1). It is also known that the destruction of active centres on the surface of, *inter al.*, palladium, by poisoning, increases the cathodic production of atomic hydrogen (Kobosew and Monblanowa, *ibid.*, 1936, **4**, 395; Farkas, *Trans. Faraday Soc.*, 1936, **32**, 1667) and the transferable overpotential.

The conclusion is reached that annealed gold forms a " non-equilibrium atomic hydrogen electrode." Its behaviour can only be explained in terms of a cathodic generation of hydrogen atoms which are unable to escape from the metal by any facile mechanism: combination, ionisation, evaporation, or electrochemical desorption. All the signs are present of a metal which becomes, over long periods, increasingly saturated with hydrogen which can only be dissipated in some slow process, or combination of processes, reflected in the slow and characteristic decay of overpotential. This statement, which summarises the main result of the present work, is of possible importance in relation to current ideas on hydrogen overpotential. It is amplified and supported in the discussion which follows.

The growth of overpotential at an annealed gold electrode has been observed oscillographically, but cannot be analysed in detail at present. It is clear, however, that during the later stages of this growth the electrode must pass through a succession of states, developing one from another. Early in this development, hydrogen atoms accumulate upon the electrode surface. The processes by which these atoms leave the surface increase in rate and, normally, this would soon establish a kinetic steady state. But if these processes are very slow, then at all but the lowest current densities the accumulation of hydrogen atoms may become extensive and lead to a progressive change in the properties of the electrode surface. This may occur by a " burning out " or obstruction of the few remaining active centres. If the rate of dissipation of hydrogen atoms has an upper limit, not dependent upon potential, there will be a critical rate of discharge. For rates of discharge less than the critical, a steady state will be possible; for higher rates, accumulation of atoms may proceed unchecked and lead to progressive saturation. Since rate of discharge is a function of cathodic potential, this is consistent with the observation that has been made that there is a critical potential attainment of which during polarisation greatly modifies subsequent electrode behaviour.

In the later stages of overpotential growth, development is slow enough to suggest the participation of bulk, rather than purely surface phenomena. It is believed that atomic hydrogen penetrates the gold lattice. Gold does not normally dissolve hydrogen (cf. Barrer, " Diffusion in and through Solids," Cambridge Univ. Press, 1951, p. 146), although silver does so. Since gold and silver have cubic close-packed structures of similar dimensions,

there seems to be no theoretical reason (cf. Fowler and Smithells, *Proc. Roy. Soc.*, 1937, *A*, **160**, 37) why hydrogen should not dissolve in gold. Recorded solubilities relate to equilibria with gaseous hydrogen under such conditions that the equilibrium concentration of hydrogen atoms is very small. Very different behaviour may be expected if the surface of the metal phase, in such a state that it is unable to catalyse atom recombination, is provided with a relatively enormous disequilibrium concentration of pre-formed hydrogen atoms. Benton's statement (*Trans. Faraday Soc.*, 1932, **28**, 202) that activated adsorption must always precede solution is perhaps relevant in this connection. This is well established by the recent proof that an evaporated film of spectroscopically pure gold, otherwise indifferent to hydrogen, takes up atomic hydrogen with avidity (Pritchard and Tompkins, personal communication), an interesting result which appears to be opposed to the view that chemisorption of hydrogen on clean metals is not activated (Eley, *J. Phys. Colloid Chem.*, 1951, **55**, 1017).

The view that bulk absorption is involved in our experiments is supported by the dependence of electrode properties, as judged by overpotential decay, on time of cathodisation and their independence of current density above a certain minimum. If these properties depend upon the amount of hydrogen absorbed, they will in turn depend solely on the period of time for which the surface concentration of hydrogen atoms has been maintained at its saturation value.

The nature of the potential changes after cathodisation also suggests a bulk phenomenon; there is a superficial resemblance to desorption isotherms of hydrogen from palladium, in which discontinuities may arise solely because of maintenance of the rate of surface desorption by faster diffusion from the interior (Ubbelohde and Egerton, *Trans. Faraday Soc.*, 1932, **28**, 284). Discontinuous overpotential decay has also been observed with platinum (Bryant and Coates, *Discuss. Faraday Soc.*, 1947, **1**, 115), tantalum, niobium, and molybdenum (Bockris, *Trans. Faraday Soc.*, 1947, **43**, 417), in which metals, with the possible exception of molybdenum, hydrogen is soluble (Smithells, "Metals Reference Book," Butterworths, 1949). It is believed that the potential changes in question do in fact represent a discontinuous desorption of hydrogen atoms. The further discussion is based upon this view.

Desorption isotherms with successive discontinuities may occur when adsorbed molecules escape from a non-uniform surface consisting of a discrete number of areas of differing heat of evaporation (Taylor, *ibid.*, 1932, **28**, 131), and some of the desorption isotherms of hydrogen from metals observed by Benton and White (*J. Amer. Chem. Soc.*, 1931, **53**, 3301) show resemblances to our potential–time curves. The loss of hydrogen atoms from a metal–solution interface, however, is likely to differ from the case of evaporation into the gas phase. On the assumption that the hydrogen atoms are firmly held at the gold surface (Farkas, *Z. phys. Chem.*, 1929, **5**, *B*, 474; Deborin and Ershler, *loc. cit.*), two mechanisms of desorption require examination.

The state of the adsorbed atoms, held by short-range forces, may be viewed in terms of Lennard-Jones's discussion (*Trans. Faraday Soc.*, 1932, **28**, 333). Each atom is held in a potential field which has a deep hollow along a normal to the surface passing through a gold atom and which is wavy in two dimensions parallel to the surface. Evaporation from the surface and migration about it are therefore both activated processes, of which migration is by far the easier. This suggests that desorption occurs mainly by recombination, which probably only takes place when two atoms meet close enough to a gold atom for the latter to act as third body. The frequency of such encounters, leading to desorption, will depend upon the two-dimensional geometry of the surface concerned in two ways; first, in an obvious way upon the geometry itself, and secondly, because the geometry largely controls the activation energy of migration. This will tend to differentiate one kind of surface from another as a substrate for the recombination reaction. Not only are markedly different specific reaction rates (*i.e.*, rates per unit surface concentration of atoms) to be expected for recombinative desorption at different crystal planes, but also different maximum rates, for each kind of plane has a different upper limit to the number of hydrogen atoms it can accommodate. This will widen the disparity between the planes. It is known that different crystal planes of metals do differ in significant properties: adsorptivity and work

function (Johnson and Shockley, *Phys. Rev.*, 1936, **49**, 436; Martin, *ibid.*, 1938, **53**, 937) and in hydrogen overpotential (Allbrecht, *Z. Elektrochem.*, 1951, **55**, 173).

Reasons have already been given for thinking that progressive bulk saturation of the gold occurs as a result of prolonged cathodisation. Whether this is due to lattice penetration, or to the entry of hydrogen atoms to interior surfaces along lattice defects or grain boundaries, a reservoir of atoms will be provided for the replenishment of the surface planes. In either case the migration of hydrogen atoms from the interior will be an activated process occurring more easily in preferred directions (cf. Barrer, *op. cit.*, p. 200), probably parallel to the crystal planes of denser packing.

Events following cathodic polarisation may be traced on the basis of these postulates. Immediately the polarising circuit is broken, activation overpotential very rapidly vanishes according to well-known laws. There may then occur a relief of a degree of surface supersaturation by evaporation of hydrogen atoms, leading to a temporary steady state, during which the rate of replenishment of hydrogen atoms is adequate to keep all surfaces operating at the maximum rate of recombinative desorption. With continued decline of the internal concentration of hydrogen atoms, however, there must eventually be a decrease in the rate of desorption. Reasons why this should occur in a non-uniform manner have already been indicated, and the simplest assumption is that rate of desorption from one kind of plane is maintained by lateral migration from another. If, however, the surface planes are replenished by diffusion from the interior, there is a further factor promoting non-uniformity. Crystal planes of low reticular density, less efficient in promoting recombinative desorption, are necessarily intersected by other planes of higher reticular density, along which migration of atoms is relatively mobile. These will serve, therefore, for the more efficient replenishment from the interior of the less active surface planes. Conversely, the surface planes of closest spacing and greatest activity can be no more, and perhaps less, efficiently replenished. Conditions may then arise where rates of recombination at the different surface planes approach equality, but at one plane rate-limitation may be due to the recombination and at another to replenishment. A steady state would then arise.

The adsorption of hydrogen atoms on metals, however, may be so strong that there is no tendency for recombinative desorption to occur (Roberts, *Trans. Faraday Soc.*, 1939, **35**, 941). Although this statement does not apply directly to the metal–solution interface, it is necessary to envisage an electrochemical desorption process as a possibly easier alternative, since the potential barrier to the removal of a hydrogen ion may be lower than that opposing the removal of an atom. There can be no doubt that hydrogen atoms adsorbed at a metal–solution interface have some tendency to ionise; the system can be regarded as an acid (Frumkin, *Z. phys. Chem.*, 1932, *A*, **160**, 116; Horiuti and Polanyi, *Acta Physicochim.*, 1935, **2**, 505), with the bare metal as the conjugate base. Different crystal planes represented in the surface will be undoubtedly of different "acid strength," and it may be supposed that ionisation occurs preferentially at an area of lower adsorption energy. But, clearly, no desorption process accompanied by a net transfer of charge will fit the case. This is avoided if a simultaneous discharge of hydrogen ions from solution occurs at an area of greater adsorption energy. This is intrinsically probable; it will be accompanied by a flow of local current within the electrode and will provide a mechanism for the stepwise loss of total hydrogen by whatever process. If, however, desorption of hydrogen as a molecule is favoured whenever a hydrogen ion is discharged at a site adjacent to an adsorbed atom, this will tend to keep the area concerned half covered with hydrogen atoms. If the extent of covering becomes less, the probability of discharge without desorption increases; if it becomes more, the reverse. This again would clearly favour the occurrence of steady states. It may be noted that the evidence of the behaviour of these annealed gold electrodes is against the occurrence of what is generally implied by "the electrochemical mechanism."

Explanation of the overpotential decay of the annealed gold electrodes in terms of these theories of hydrogen-atom desorption involves the assumption already tacitly made that the hydrogen atoms are potential-determining, but not in accordance with the Nernst equation. This is consistent with the basic postulate that a non-equilibrium atomic

hydrogen electrode is involved, for the Nernst equation can apply only to a system in equilibrium.

The results of this preliminary work and its interpretation raise a number of points of interest that require further investigation. Although atomic hydrogen plays a minor part in current theories of hydrogen overpotential and cathodic hydrogenation, its essential participation in many striking phenomena at electrodes other than palladium cannot be doubted (as, for example, in the remarkable " iron pillow " experiment of Fink, Urey, and Lake, *J. Chem. Physics*, 1934, **2**, 105). It is possible that atomic hydrogen should receive more general attention in this connection. This view was emphasised some years ago (Hickling and Salt, *Trans. Faraday Soc.*, 1942, **38**, 474) and can still be supported. It is hoped to follow this matter in a further communication.

Experimental

The preparation of materials and experimental procedure were as described in the preceding paper, except for the following. The solution-preparation flask was fitted with an ancillary gold electrode at which pre-electrolysis was carried out, 850 coulombs being passed, under suitable conditions, in the course of 24 hr. The solution was then transferred to the cell by hydrogen pressure. Further pre-electrolysis of the solution in the cell (20 coulombs in 20 hr.) was then conducted by means of a second ancillary gold electrode, replacing the platinised platinum electrode in compartment *B* (cf. Fig. 3 of preceding paper).

The authors record their thanks to Dr. F. C. Tompkins, F.R.S., for information kindly provided before publication, and to Dr. R. W. Pittman for constant helpful discussion. One of them (S. S.) thanks the Authorities of Patna University for a study grant.

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The Characteristic Infrared Absorption of the Methyl Rocking Vibrations of Aromatic Methyl Groups.

By R. R. Randle and D. H. Whiffen.

[Reprint Order No. 6417.]

Evidence is presented that the CH_3 rocking modes of isolated aromatic methyl groups absorb near 1042 cm.$^{-1}$ and that the vibration is probably degenerate. For two adjacent methyl groups frequencies near 990 and 1021 cm.$^{-1}$ are suggested, and the more highly methylated compounds are considered.

Some of the more troublesome frequencies to assign in many molecules are the CH_3 rocking frequencies which are external group vibrations in Sheppard and Simpson's sense (*Quart. Rev.*, 1953, **7**, 19) and are therefore liable to vary with the nature of the residue to which the methyl group is attached. The range 950—1150 cm.$^{-1}$ covers the majority of assignments (Torkington, *J. Chem. Phys.*, 1950, **18**, 768; Brown and Sheppard, *Trans. Faraday Soc.*, 1954, **50**, 1164, etc.), and a characteristic methyl frequency near 967 cm.$^{-1}$, when the group is attached to a *cyclo*hexane or to a sugar ring, has been assigned to this mode (Barker, Bourne, Stephens, and Whiffen, *J.*, 1954, 4211).

In toluene derivatives in which the methyl group is attached to a more rigid skeleton than in aliphatic compounds, there is a greater probability that the group frequency will be more constant. Pitzer and Scott (*J. Amer. Chem. Soc.*, 1943, **65**, 803) have tentatively assigned frequencies in the range 1000—1200 cm.$^{-1}$ to the rocking vibrations, but admit that the evidence for the detailed assignments is weak. The frequencies to be expected for benzene derivatives in general have recently been discussed (Randle and Whiffen, " Molecular Spectroscopy," Report on the conference held in London in October 1954 by the Institute of Petroleum) and relevant spectra have been examined to see what extra infrared absorption appears when methyl groups are present.

In compounds with a methyl group and no substituent in either of the adjacent *ortho*-positions in the ring, a band of moderate intensity appears near 1042 cm.$^{-1}$ and some examples are given in Table 1. *meta*-Disubstituted benzenes are excluded as these have a

TABLE 1. *Isolated methyl groups: Table of frequency of absorption (in cm.$^{-1}$), maximum extinction coefficient (in cm.^{2} molecule^{-1} log$_e$), and band width at half height (in cm.$^{-1}$).*

	ν (cm.$^{-1}$) *	$10^{20}E_{max.}$	$\Delta\nu_{1/2}$		ν (cm.$^{-1}$) *	$10^{20}E_{max.}$	$\Delta\nu_{1/2}$
Toluene	1041	4·0	22	*p*-Chlorotoluene...	1042	6·1	16
p-Xylene	1042	7·4	18	*p*-Bromotoluene...	1041	5·8	*ca.* 17
Mesitylene [a]	1037 †	—	—	*p*-Iodotoluene ...	1040	5·5	*ca.* 17
p-Fluorotoluene ...	1042	4·0	18				

* In CS_2 solution, except † which is for liquid.
[a] A.P.I. project No. 44, " Catalogue of Infrared Spectra."

ring C–H deformation expected near 1045 cm.$^{-1}$ (Randle and Whiffen, *loc. cit.*) which masks the methyl absorption.

There is no evidence to show whether this is the in-plane or the out-of-plane methyl rocking; indeed, it is by no means certain that the six-fold potential-energy barrier opposing internal rotation of the methyl group relative to the phenyl ring is large enough to remove the degeneracy which is present in such compounds as methyl chloride in which the attached group is cylindrically symmetrical. Pitzer (*Discuss. Faraday Soc.*, **1951**, **10**, 66) quotes 500 $\pm$ 500 cal. as the best value for toluene, though this may well be many times too high in view of the observed value of only 6 cal. for nitromethane (Tannenbaum, Johnson, Myers, and Gwinn, *J. Chem. Phys.*, **1954**, **22**, 949) which has a similar six-fold barrier. A search failed to reveal any possibilities for a second methyl rocking frequency although it is difficult to be satisfied of its absence since in most of the spectra the range 900—1150 cm.$^{-1}$ contains many absorption bands. In mesitylene (1 : 3 : 5-trimethylbenzene), whose symmetry reduces the number of absorption bands considerably, there is no unassigned absorption band of comparable intensity to that at 1037 cm.$^{-1}$, although it might be expected that one in-plane (degenerate) and one out-of-plane rocking mode should be active in the infrared and that the dipole-moment gradients, which govern the intensity, should be similar. Some of the compounds of Table 1 have been measured in carbon disulphide solution and their peak intensities and band widths are given. They are only approximate, as overlapping by neighbouring bands is serious in some cases. The band widths are exceptionally large and must be compared with the many neighbouring bands for these same solutions which are seldom over 10 cm.$^{-1}$ wide at half intensity. This is perhaps further evidence that the degeneracy is not quite lifted by the phenyl group.

ortho-Substituents are likely to raise the potential barrier (Pitzer, *loc. cit.*, quotes 2000 cal. for *o*-xylene), and if the substituent is a second methyl group symmetric and anti-symmetric rocking vibrations will arise. Table 2 gives some further compounds and

TABLE 2. *Adjacent methyl groups.*

Two adjacent Me groups	Frequency (cm.$^{-1}$)
o-Xylene [a]	985, 1022, 1053
1 : 2 : 4-Trimethylbenzene [a]	999, 1021, 1038
1 : 2 : 4 : 5-Tetramethylbenzene [a]	1000, 1022
More than two adjacent Me groups	
1 : 2 : 3-Trimethylbenzene [a]	988, 1010
1 : 2 : 3 : 4-Tetramethylbenzene [a]	1005, 1040, 1065
1 : 2 : 3 : 5-Tetramethylbenzene [a]	990, 1010, 1035, 1076
Pentamethylbenzene [b]	997, 1011, 1031, 1072
Hexamethylbenzene [b]	989, 1063

[a] A.P.I. project No. 44, " Catalogue of Infrared Spectra." [b] In CS_2 (Whiffen, Thesis, Oxford, 1946).

their absorption frequencies in this region although some of these may be due to in-plane ring C–H deformations. Although it is unwise to generalize on three cases, there is evidence for absorption near 995 and 1022 cm.$^{-1}$ for *ortho*-dimethyl compounds without further substituents adjacent to the methyl groups.

Hexamethylbenzene has three strong infrared bands between 500 and 1300 cm.$^{-1}$,

viz., at 1063, 988, and 793 cm.$^{-1}$, which can reasonably be attributed to the in-plane and the out-of-plane methyl rocking and the E_{1u} C–CH_3 stretching. An approximate calculation, treating the methyl group as a point mass of 15 with a C–CH_3 stretching constant of $4{\cdot}5 \times 10^5$ dynes/cm. (Herzberg, "Infra-red and Raman Spectra," van Nostrand, 1945, p. 193) and with other constants transferred from benzene, led to E_{1u} frequencies of 1490 cm.$^{-1}$ (ring C–C stretching), 850 cm.$^{-1}$ (C–CH_3 stretching), and less than 350 cm.$^{-1}$ (C–CH_3 deformation). It seems reasonable to suppose that the observed band at 793 cm.$^{-1}$ is the C–CH_3 stretching, that at 988 cm.$^{-1}$ the out-of-plane methyl rocking, and that at 1063 cm.$^{-1}$ is the in-plane methyl rocking, which is taken to be the higher since it will involve greater van der Waals repulsion. The arguments of this paragraph are fully supported by the assignment by Mann and Thompson (*Proc. Roy. Soc.*, 1952, *A*, **211**, 168), who used oriented crystals of hexamethylbenzene and polarised radiation.

Experimental.—The carbon disulphide solutions were measured on a Grubb-Parsons single-beam spectrometer with slits of 0·12 mm., cell length 1·1 mm., and concentrations of 2% v/v or less.

We thank Professor H. W. Melville, F.R.S., for his interest in the work, and the National Coal Board for sponsoring our programme on the infrared spectra of aromatic compounds. We also thank a Referee who drew our attention to the work of Mann and Thompson (*loc. cit.*).

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Experiments on the Synthesis of Bz-*Substituted Indoles and Tryptophans. Part III.* The Synthesis of the Four* Bz-*Chloro-indoles and -tryptophans.*

By H. N. Rydon and J. C. Tweddle.

[Reprint Order No. 6439.]

Syntheses of the four *Bz*-chloroindoles and the four *Bz*-chlorotryptophans are described.

The four *Bz*-chloroindoles and the derived *Bz*-chlorotryptophans were required for biochemical studies, in extension of earlier work on the corresponding methyl compounds (Fildes and Rydon, *Brit. J. Exp. Path.*, 1947, **28**, 211), and the synthesis of these compounds is described below; † the biochemical work will be reported elsewhere.

When our work began, neither the monochloroindoles nor the monochlorotryptophans were known, but, while it was in progress, Uhle (*J. Amer. Chem. Soc.*, 1949, **71**, 761) described the synthesis of 4-chloroindole and Fox and Bullock (*ibid.*, 1951, **73**, 2756) that of 6-chloroindole, although, in view of the prior publication of Rydon and Long (*Nature*, 1949, **164**, 575), the latter authors did not record an analysis; attention may also be drawn to the recent synthesis of the four *Bz*-fluoroindoles (Allen, Brunton, and Suschitzky, *J.*, 1955, 1283).

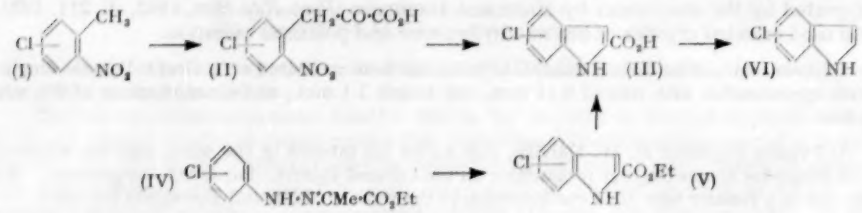
All four chloroindoles were prepared by way of the chloroindole-2-carboxylic acids (III). In the 4- and 6-chloro-series, these were prepared by Reissert's method (*Ber.*, 1897, **30**, 1030; cf. Blaikie and Perkin, *J.*, 1924, **125**, 296; Uhle, *loc. cit.*), the appropriate chloronitrotoluene (I) being condensed with ethyl oxalate; reductive cyclisation of the resulting chloronitrophenylpyruvic acids (II) gave the indole acids (III); potassium ethoxide was superior to sodium ethoxide in the condensation with ethyl oxalate, giving better, and

* Part II, Rydon and Siddappa, *J.*, 1951, 2462.

† All four *Bz*-chloroindoles and the derived chlorotryptophans were synthesised, during 1948—52, by Mr. C. A. Long, working in collaboration with one of us (H. N. R.) at Birkbeck College, London; unfortunately, however, apart from the small amount of work incorporated in the Experimental section, the detailed records of this work have been lost and the present study is virtually a complete re-investigation.

more consistent, yields of the pyruvic acid (II). For the preparation of 5- and 7-chloroindole, the ethyl pyruvate chlorophenylhydrazones (IV) were cyclised to the esters (V), which were then hydrolysed to the required acids (III); polyphosphoric acid (Snyder and Xerber, *J. Amer. Chem. Soc.*, 1950, **72**, 2962, 2965) was found to be greatly superior to other reagents for the cyclisation, giving better yields of purer products (cf. Kissman, Farnsworth, and Witkop, *ibid.*, 1952, **74**, 3948).

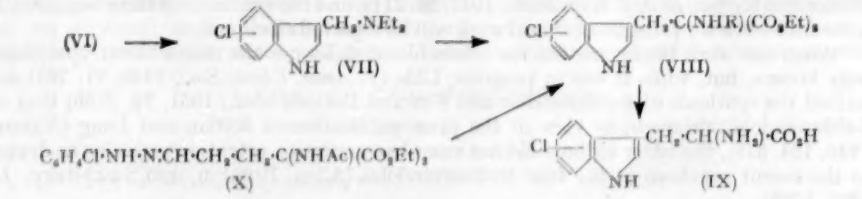
Both routes involve, as the final stage, the decarboxylation of the chloroindole-2-carboxylic acid (III). Uhle (*loc. cit.*) obtained a good yield of 4-chloroindole by heating the 4-chloro-acid (III) with cuprous chloride in quinoline and the same method was used



by Fox and Bullock (*loc. cit.*) for the preparation of 6-chloroindole, although no yield is recorded. In our hands this method was unsatisfactory, giving variable yields which were usually very low; Barltrop and Taylor (*J.*, 1954, 3399) experienced even greater difficulty in the decarboxylation of 4- and 6-bromoindole-2-carboxylic acid. Replacement of cuprous chloride by the chromite gave better, but still variable, yields; the variability was finally traced to the presence of small amounts of sulphate in the acid (III) and decarboxylation of the chloroindole-2-carboxylic acids (III), carefully freed from sulphate, by heating in quinoline in the presence of copper chromite has given the chloroindoles (VI) in consistent yields of 60—70%.

In this, as in the fluoro-series (Allen, Brunton, and Suschitzky, *loc. cit.*), the 4-halogenoindole is much lower-melting than its isomerides.

For the synthesis of 4- and 6-chlorotryptophan * (IX) we used Hellmann's modification (*Z. physiol. Chem.*, 1949, **284**, 163) of the gramine synthesis of tryptophan. The chloroindoles (VI) were condensed with formaldehyde and diethylamine, yielding the 3-diethylaminomethyl compounds (VII); condensation with formamidomalonic ester yielded the



(chloroindolylmethyl)formamidomalonic esters (VIII; R = CHO) which were smoothly hydrolysed and decarboxylated to the chlorotryptophans (IX). This route was much superior to the original gramine synthesis (Snyder and Smith, *J. Amer. Chem. Soc.*, 1944, **66**, 350; Albertson, Archer, and Suter, *ibid.*, p. 500; 1945, **67**, 36) used for the synthesis of the *Bz*-methyltryptophans (Rydon, *J.*, 1948, 705). 5- and 7-Chlorotryptophan were synthesised from the corresponding chlorophenylhydrazines, by way of the chlorophenylhydrazones (X), by the procedure of Warner and Moe (*J. Amer. Chem. Soc.*, 1948, **70**, 2763, 2765).

* While this paper was being prepared for publication, Hardegger and Corrodi (*Helv. Chim. Acta*, 1955, **38**, 468) described the synthesis of 4-chlorotryptophan by the same method; their results are in general agreement with ours.

Experimental

Chloroindoles.

Polyphosphoric acid was prepared by dissolving phosphoric oxide (360 g.) in commercial orthophosphoric acid, *d* 1·75 (200 g.).

4-*Chloroindole.*—A mixture of 2-chloro-6-nitrotoluene (100 g.) and ethyl oxalate (80 g.) was added during 10—15 min. to ethanolic potassium ethoxide (from potassium, 28 g., and anhydrous ethanol, 320 ml.), the temperature being kept at 15—20°. The mixture was then refluxed for 30 min. and the ethanol removed under reduced pressure. After dilution with water, unchanged starting material was removed by steam-distillation. Acidification of the filtered residue precipitated 2-chloro-6-nitrophenylpyruvic acid (II) (57·6 g., 41%); a specimen crystallised from benzene in needles, m. p. 116° (Uhle, *loc. cit.*, gives m. p. 114—115°).

This acid (40 g.) was reduced as described by Uhle (*loc. cit.*); the crude product, twice washed with water, was suspended in very dilute hydrochloric acid containing a little barium chloride and extracted with ether. Evaporation of the ether, after repeated washing with water until free from sulphate, left 4-chloroindole-2-carboxylic acid (III) (29 g., 90%), which crystallised from aqueous ethanol in long needles, m. p. 264° (decomp.) (Uhle, *loc. cit.*, gives m. p. 259—260°). An intimate mixture of the unrecrystallised, sulphate-free acid (20 g.) and copper chromite (2 g.) (Vogel, "Practical Organic Chemistry," Longmans, Green and Co., London, 2nd Edn., 1951, p. 808), suspended in redistilled quinoline (100 ml.), was heated to 215° (internal temp.) for 2 hr. The product was poured into water and repeatedly extracted with ether; the extract was washed (2N-hydrochloric acid, 2N-sodium hydrogen carbonate, water), dried (Na_2SO_4), and distilled, affording 4-chloroindole (VI) (10·3 g., 67%), b. p. 106—108°/0·6 mm., n_D^{20} 1·6278 (Uhle, *loc. cit.*, gives b. p. 143°/10 mm., n_D^{20} 1·6254; Fox and Bullock, *loc. cit.*, b. p. 150°/13 mm., n_D^{20} 1·6286).

5-*Chloroindole.*—A well-stirred mixture of ethyl α-methylacetoacetate (50 g.) and ethanol (250 ml.) was treated at 0° with 50% potassium hydroxide solution (130 g.); crushed ice (200 g.) and a diazonium solution, from *p*-chloroaniline (45 g.), 10N-hydrochloric acid (160m l.), and sodium nitrite (45 g.), were then added, with continued stirring. The brick-red solid which separated after 10 min. was collected and recrystallised from 50% aqueous ethanol (charcoal), affording ethyl pyruvate *p*-chlorophenylhydrazone (IV) (55 g., 65%), needles, m. p. 138° (Hewitt, *J.*, 1893, **63**, 868, gives m. p. 138°).

This hydrazone (10 g.) was dissolved, with stirring, in polyphosphoric acid (20 g.) and the viscous solution slowly heated, with continued stirring, in a metal-bath until a sudden rise in the internal temperature (from 150° to 180°) took place; the temperature of the mixture was maintained at 180° for a further 5 min. and then allowed to fall to 60°, whereupon water (100 ml.) was added. Extraction with ether, followed by evaporation of the extract, after washing with 5% sodium hydrogen carbonate solution and water, afforded *ethyl 5-chloroindole-2-carboxylate* (V) (5 g., 54%), which crystallised from ethanol in needles, m. p. 167—168° (Found: C, 59·35; H, 4·65; N, 6·3. $C_{11}H_{10}O_2NCl$ requires C, 59·1; H, 4·5; N, 6·3%). The crude ester (40 g.) was refluxed for 2 hr. with ethanolic potassium hydroxide (22 g. in 250 ml.); pouring the mixture into dilute hydrochloric acid precipitated *5-chloroindole-2-carboxylic acid* (III) (27·5 g., 79%) which, recrystallised from 50% aqueous ethanol, had m. p. 289—290° (decomp.) (Found: C, 55·2; H, 3·2; N, 7·1. $C_9H_6O_2NCl$ requires C, 55·3; H, 3·1; N, 7·15%).

This acid (4·2 g.) was decarboxylated at 215° for 2 hr. as described for the 4-isomer. The fraction, b. p. 120—130°/0·4 mm. (2.0 g., 62%), solidified (m. p. 66—68°) and was sufficiently pure for preparative purposes; recrystallisation from light petroleum (b. p. 40—60°) gave pure *5-chloroindole* (VI) as silvery plates, m. p. 71—72° (Found: C, 63·4; H, 4·05; N, 8·5. C_8H_6NCl requires C, 63·4; H, 3·95; N, 9·25%); the *picrate* crystallised from benzene in orange plates, m. p. 147° (Found: C, 44·5; H, 2·4; N, 15·1. $C_{14}H_9O_7N_4Cl$ requires C, 44·2; H, 2·35; N, 14·7%).

6-*Chloroindole.*—4-Chloro-2-nitrotoluene (22 g.) was condensed with ethyl oxalate (20·5 g.) in ethanolic potassium ethoxide (from potassium, 6·25 g., and anhydrous ethanol, 75 ml.), as described for 2-chloro-6-nitrotoluene; *4-chloro-2-nitrophenylpyruvic acid* (II) (13 g., 42%) crystallised from benzene in needles, m. p. 136° (Found: C, 44·6; H, 2·4; N, 5·8. $C_9H_6O_5NCl$ requires C, 44·4; H, 2·5; N, 5·75%).

This acid (40 g.) in dilute ammonia solution was added to a suspension in water (1 l.) of ferrous hydroxide, from ferrous sulphate heptahydrate (280 g.) and ammonia solution (*d* 0·880; 170 ml.), and the mixture boiled and stirred for 10 min. Ferric hydroxide was removed and

washed with dilute ammonia solution until the washings gave no precipitate on acidification. Acidification of the filtrate and washings with hydrochloric acid precipitated 6-chloroindole-2-carboxylic acid (III) (27·4 g., 85%), which crystallised from aqueous ethanol in granules, m. p. 242° (decomp.) (Found: C, 55·4; H, 3·1; N, 7·7. Calc. for $C_9H_6O_2NCl$: C, 55·3; H, 3·1; N, 7·2%) (Fox and Bullock, *loc. cit.*, give m. p. 242—244°).

This acid (10 g.), freed from sulphate as described for the 4-chloro-compound, was similarly decarboxylated at 210—220° for 3 hr., affording *6-chloroindole* * (VI) (5·1 g., 66%), b. p. 110°/0·2 mm., leaflets, m. p. 86—87° [from light petroleum (b. p. 60—80°)] (Found: C, 63·7; H, 3·8; N, 9·7. C_8H_6NCl requires C, 63·4; H, 3·95; N, 9·25%). (With C. A. Long) The *picrate* had m. p. 143—144° (Found: C, 44·0; H, 2·6; N, 15·4; Cl, 9·0. $C_{14}H_9O_7N_4Cl$ requires C, 44·2; H, 2·35; N, 14·7; Cl, 9·3%).

7-Chloroindole.—Pyruvic acid *o*-chlorophenylhydrazone (65 g.) (Hewitt, *J.*, 1891, **59**, 209) was esterified by passing dry hydrogen chloride through its ethanol solution for 4 hr.; the ester (IV) (55 g., 75%) crystallised from the mixture in needles, m. p. 71° (Hewitt, *J.*, 1893, **63**, 868, gives m. p. 68°). This ester (25 g.) was cyclised with polyphosphoric acid (40 g.) at 190°, as described for the 5-chloro-compound; *ethyl 7-chloroindole-2-carboxylate* (V) (12 g., 52%) crystallised from ethanol in needles, m. p. 105° (Found: C, 59·5; H, 4·3; N, 6·1. $C_{11}H_{10}O_2NCl$ requires C, 59·1; H, 4·5; N, 6·3%). Hydrolysis, as described for the 5-chloro-compound, afforded *7-chloroindole-2-carboxylic acid* (III) (91% yield) which, crystallised from 30% ethanol, had m. p. 234—236° (decomp.) (Found: C, 54·95; H, 3·1; N, 7·2. $C_9H_6O_2NCl$ requires C, 55·3; H, 3·1; N, 7·15%).

This acid (4·8 g.) was decarboxylated at 215° for 2 hr., as described for the 4-chloro-compound. Recrystallisation of the fraction, b. p. 90—95°/0·25 mm., m p. 54° (2·6 g., 70%), from light petroleum (b. p. 40—60°) yielded *7-chloroindole* (VI) as silvery plates, m. p. 57—58° (Found: C, 63·5; H, 4·3; N, 8·6. C_8H_6NCl requires C, 63·4; H, 3·95; N, 9·25%); the *picrate* crystallised from benzene in orange plates, m. p. 154—155° (Found: C, 44·2; H, 2·35; N, 14·8. $C_{14}H_9O_7N_4Cl$ requires C, 44·2; H, 2·35; N, 14·7%).

Chlorotryptophans.

4-Chlorotryptophan.—40% Aqueous formaldehyde (3·3 ml.) was added to a mixture of diethylamine (3·1 g.) and 60% aqueous acid (9 ml.), prepared at below 3°. This mixture was poured into 4-chloroindole (6·5 g.), which dissolved on warming to room temperature. After 2 hr. the mixture was poured into 2N-sodium hydroxide (150 ml.) and the white curdy precipitate immediately isolated by filtration; *4-chloro-3-diethylaminomethylindole* (VII) (10 g.; 99%) so prepared crystallised from acetone in prisms, m. p. 130° (Found: C, 65·7; H, 6·9; N, 11·8. $C_{13}H_{17}N_2Cl$ requires C, 66·0; H, 7·2; N, 11·85%). The amine (VII) (5·9 g.) and diethyl formamidomalonate (6 g.) (Galat, *J. Amer. Chem. Soc.*, 1947, **69**, 965) were added to a suspension of sodium hydroxide (0·35 g.) in boiling toluene (25 ml.); the mixture was heated under reflux at 130° in a stream of dry nitrogen for 30 min. After cooling to 0°, the semi-solid product was filtered off and washed with a little toluene; *diethyl (4-chloro-2-indolylmethyl)formamidomalonate* (VIII; R = CHO) (8·0 g., 88%) crystallised from ethanol in leaflets, m. p. 202° (Found: C, 56·2; H, 4·9; N, 7·3. $C_{17}H_{19}O_5N_3Cl$ requires C, 55·65; H, 5·2; N, 7·65%). This ester (4·5 g.) was heated under reflux in an oil-bath at 120° with sodium hydroxide (2·28 g.) in water (22 ml.) for 7 hr.; after cooling, glacial acetic acid (4 ml.) was added and the mixture heated for a further 2 hr. at 130°. *4-Chlorotryptophan* (IX) (1·8 g., 61%) separated overnight at 2° and recrystallised from glacial acetic acid as feathery clusters of plates, m. p. 298° (decomp.) (Found: C, 54·8; H, 4·35; N, 11·4. $C_{11}H_{11}O_2N_2Cl$ requires C, 55·3; H, 4·6; N, 11·7%).

Dimethyl sulphate (12·2 g.) was added during 5 min. to a solution of diethyl acetamidomalonate (10 g.) and 4-chlorogramine (9 g.) (Fox and Bullock, *loc. cit.*) in ethanolic sodium ethoxide (from sodium, 1·0 g., and anhydrous ethanol, 120 ml.). After the mixture had been kept at room temperature for 24 hr. it was filtered and the filtrate poured into water (500 ml.); the precipitated *diethyl (4-chloroindolylmethyl)acetamidomalonate* (VIII; R = Ac) (7·8 g., 47·5%) was collected and recrystallised from ethanol, forming laminæ, m. p. 162° (Found: C, 56·6; H, 5·3; N, 7·4. $C_{18}H_{21}O_5N_2Cl$ requires C, 56·8; H, 5·5; N, 7·35%).

5-Chlorotryptophan.—*p*-Chlorophenylhydrazine (30 g.) and glacial acetic acid (4·5 ml.) were added to a benzene solution of γ-acetamido-γγ-diethoxycarbonyl-*n*-butaldehyde (from acraldehyde, 17·1 ml., and diethyl acetamidomalonate, 5·5 g.; Warner and Moe, *loc. cit.*). The

* In a paper which appeared while our manuscript was in preparation, Plieninger *et al.* (*Chem. Ber.*, 1955, **88**, 370) record m. p. 78—80°.

mixture was warmed to 50° for 1 hr. and then kept at 2° for 24 hr. Evaporation to half volume under reduced pressure in an atmosphere of nitrogen, followed by addition of aqueous ethanol (70% v/v), precipitated *γ-acetamido-γγ-diethoxycarbonyl*-n-*butaldehyde* p-*chlorophenylhydrazone* (X) (60 g., 72%) which, crystallised from light petroleum (b. p. 60—80°), had m. p. 94—95° (Found: C, 54·7; H, 5·8; N, 10·7. $C_{18}H_{24}O_5N_3Cl$ requires C, 54·4; H, 6·0; N, 10·6%).

The crude hydrazone (50 g.) was refluxed under nitrogen with 5% sulphuric acid (200 ml.) for 5 hr. After the mixture had been kept overnight at 2°, the solidified cyclisation product (VIII; R = Ac) (theoretical yield) was collected; recrystallisation from aqueous ethanol gave a product, m. p. 149—150° not depressed on admixture with material prepared by the gramine route (see below). The crude product (5 g.) was refluxed for 6 hr. with 1·5N-hydrochloric acid (30 ml.); tar was removed by filtration and the filtrate brought to pH 6·5 with 2N-sodium hydroxide. *5-Chlorotryptophan* (IX) (1·02 g., 33%) separated slowly and was recrystallised from glacial acetic acid, forming lustrous plates, m. p. 278—279° (decomp.) (Found: C, 55·2; H, 4·5; N, 11·9%).

(With C. A. Long) Condensation of 5-chloroindole (1·8 g.) with formaldehyde and dimethylamine by the procedure described below for the 6-chloro-compound afforded *5-chloro-3-dimethylaminomethylindole* (2·1 g., 85%), which crystallised from ethyl acetate in needles, m. p. 150° (Found: N, 13·85, 13·1. $C_{11}H_{13}N_2Cl$ requires N, 13·4%). Condensation of this 5-chlorogramine with diethyl acetamidomalonate, as described below for the 6-chloro-compound, yielded *diethyl acetamido-(5-chloro-2-indolylmethyl)malonate* (VIII; R = Ac), m. p. 149—150° after recrystallisation from aqueous ethanol (Found: C, 56·5; H, 5·5; Cl, 9·3. $C_{18}H_{21}O_5N_2Cl$ requires C, 56·8; H, 5·5; Cl, 9·3%).

6-Chlorotryptophan.—6-Chloroindole (6·5 g.) was condensed with formaldehyde and diethylamine, as described for the 4-chloro-compound. The product, which separated as an oil in water, was extracted with ether. Evaporation of the dried extract afforded *6-chloro-3-diethylaminomethylindole* (VII) (6·6 g., 65%) which, crystallised from light petroleum (b. p. 60—80°), had m. p. 96° (Found: N, 12·0. $C_{13}H_{17}N_2Cl$ requires N, 11·85%). Condensation of this base (5·9 g.) with diethyl formamidomalonate (6 g.), as described for the 4-chloro-compound (time of heating, 1 hr.), afforded *diethyl (6-chloro-2-indolylmethyl)malonate* (VIII; R = CHO) (6·3 g., 69%), leaflets (from ethanol), m. p. 168° (Found: C, 55·9; H, 4·9; N, 7·9. $C_{17}H_{19}O_5N_2Cl$ requires C, 55·65; H, 5·2; N, 7·65%). This ester (4·5 g.), hydrolysed and decarboxylated as described for the 4-chloro-compound, afforded *6-chlorotryptophan* (IX) (2·5 g., 85%), plates (from water), m. p. 285—286° (decomp.) (Found: C, 54·8; H, 4·6; N, 12·0%).

Aqueous dimethylamine (33% w/v; 9 g.), cooled in a freezing mixture, was treated successively with glacial acetic acid (9 ml.) and 40% aqueous formaldehyde (9 ml.), the temperature being kept below −5°. The resulting mixture was poured on to 6-chloroindole (10 g.), which dissolved on warming to 20°. After 4·5 hr. at room temperature, the mixture was poured into an excess of 2N-sodium hydroxide, the temperature being kept below 0°. After 1 hr. in a freezing mixture, the precipitated *6-chloro-3-dimethylaminoethylindole* (11·4 g., 83%) was collected and recrystallised from aqueous ethanol, forming clusters of leaflets, m. p. 132° (Found: C, 63·3; H, 6·15; N, 13·2. $C_{11}H_{13}N_2Cl$ requires C, 63·3; H, 6·25; N, 13·4%). Crude 6-chlorogramine (9·5 g.) was condensed with diethyl acetamidomalonate (9·5 g.) as described for the 4-chloro-compound; the resulting *diethyl acetamido-(6-chloro-2-indolylmethyl)malonate* (VIII; R = Ac) (8·5 g., 49%) (from aqueous ethanol) had m. p. 197—199° (Found: C, 56·4; H, 5·4; N, 7·35. $C_{18}H_{21}O_5N_2Cl$ requires C, 56·8; H, 5·5; N, 7·35%).

7-Chlorotryptophan.—*γ-Acetamido-γγ-diethoxycarbonyl*-n-*butaldehyde* o-*chlorophenylhydrazone* (X), prepared in 66% yield (crude) from *o*-chlorophenylhydrazine as described for the *p*-compound and crystallised from light petroleum (b. p. 60—80°), had m. p. 98—100° (Found: C, 54·1; H, 5·7; N, 10·4. $C_{18}H_{24}O_5N_3Cl$ requires C, 54·4; H, 6·0; N, 10·6%). The crude material was cyclised and the crude cyclisation product hydrolysed and decarboxylated as described for the 5-chloro-compound. *7-Chlorotryptophan* (IX) (40% yield) so obtained crystallised from acetic acid in plates, m. p. 291—292° (Found: C, 55·8; H, 4·6; N, 11·1%).

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The Stereochemistry of the Tropane Alkaloids. Part VI. The Configuration of the Nitrogen Atom in Tropane-3α : 6β-diol, Oscine, and the Derived Quaternary Salts.*

By Gábor Fodor, József Tóth, and Irén Vincze.

[Reprint Order No. 6003.]

The ester salt from (±)-tropane-3α : 6β-diol and ethyl iodoacetate readily gave a lactone salt, whereas the ester salt from (±)-*N*-ethoxycarbonylmethylnortropane-3α : 6β-diol and methyl iodide was incapable of lactonising. This selectivity of quaternisation, producing *N*-epimers, is contrasted with the behaviour of oscine and noroscine, and is discussed in terms of the Pitzer effect and of the possibility of hydrogen-bonding. Definite configurations are ascribed to the nitrogen atoms in a number of the compounds discussed.

The steric orientation of the oxygen-containing functional groups at $C_{(2)}$, $C_{(3)}$, and $C_{(6/7)}$ in the tropane alkaloids, relative to the —NMe bridge as a whole, has already been established (Parts I—V of this series). In subsequent investigations tropan-3β-ol (for nomenclature see Part I, *J.*, **1953**, **721**) was found to give with ethyl iodoacetate a single quaternary salt, *N*-ethoxycarbonylmethyl-3β-hydroxytropanium iodide [Scholtz and Bode (*Arch. Pharm.*, 1904, **242**, 568) earlier obtained only one of the two possible *N*-epimers from the quaternisation of tropine, atropine, brucine, and strychnine]. However, nortropan-3β-ol furnished, *via* *N*-ethoxycarbonylmethylnortropan-3β-ol and quaternisation with methyl iodide, a different, obviously *N*-epimeric form of the tropanium iodide. These stereoisomers had different crystal forms, melting points, solubilities and Debye-Scherrer diagrams (Fodor, Meeting Hungarian Chem. Soc., Szeged, September 18th, 1952; cf. Fodor, Koczka, and Lestyán, *Magyar Kém. Folyóirat*, 1953, **59**, 243). Similarly, tropine and ethyl iodide gave a salt different from that arising from *N*-ethylnortropine and methyl iodide (Tóth, Meeting Hungarian Chem. Soc., Debrecen, September 27th, 1953; Fodor, Lestyán, Tóth, and Vincze, *Vegyipari Kutató Intézetek Közleményei*, 1954, **4**, 293; Fodor, *Experientia*, 1955, **11**, 129), a result at variance with the findings of Findlay (*J. Amer. Chem. Soc.*, 1953, **75**, 3204) who claimed to have obtained the same salt by both methods, although he found *N*-propylnortropine and ethyl iodide to give a salt isomeric with that from *N*-ethylnortropine and propyl iodide. This special problem will be discussed later.

The formation, in fairly good yields and with none of the *N*-epimers, of lactone iodide such as (III), *via* the ester salt (II), from ethyl iodoacetate and (±)-tropane-3α : 6β-diol (I), (±)-oscine (VII*a*), or teloidine has been regarded previously as definite evidence for the β-orientation of the functional groups on the *endo*ethylene bridge of these alkaloids (Part V, *loc. cit.*). It also indicates the relative configuration of the asymmetric nitrogen atom in these quaternary lactone salts, the $-CH_2{\cdot}CO-$ groups being oriented towards the pyrrolidine ring, the methyl group in the opposite direction. Von Braun degradation of the base (I) to the previously unknown (±)-nortropane-3α : 6β-diol (IV), followed by treatment with ethyl iodoacetate, gave (±)-*N*-ethoxycarbonylmethylnortropane-3α : 6β-diol (V*b*) which with methyl iodide gave the salt (VI*b*), the *N*-epimer of (II). Acid hydrolysis of the ester (V*b*) gave only *N*-carboxymethylnortropane-3α : 6β-diol hydrochloride (V*a*) which showed no tendency to lactonise, a fact which points to its being *Na*-carboxymethylnortropane-3α : 6β-diol hydrochloride.† Further, the methiodide (VI*b*), in contrast to its *N*-epimer (II), could not be transesterified to the lactone (III). Hydrolysis of the ester (VI*b*) to the betaine, and treatment of the latter with hydriodic acid, gave no trace of lactone (III), most of the material being converted into the salt of the hydroxy-carboxylic acid (VI*a*).

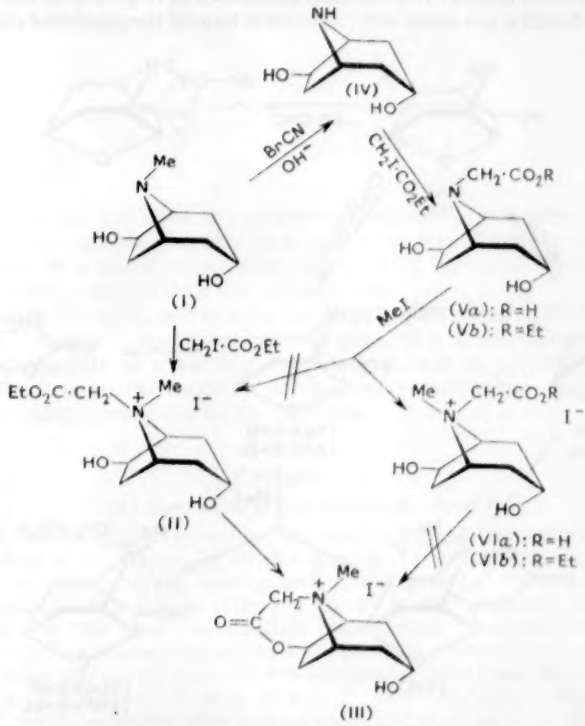
Thus, the methiodide is certainly *Na*-ethoxycarbonylmethyl-3α : 6β-dihydroxytropanium

* Part V, *Helv. Chim. Acta*, 1953, **37**, 907.

† The use of "α" and "β" to indicate the configurations of hydroxyl groups will be familiar from previous papers in this series. The further convention is now proposed, that substituents on the nitrogen atom which are directed towards the piperidine ring [see, for example, (II)] be given the prefix "*a*," and those directed to the pyrrolidine ring the prefix "*b*."

iodide (VI*b*), this being the first reported determination of the configuration of a quaternary ammonium salt. The method used should be capable of extension.

The question arises, whether knowledge of the configurations of the quaternary salts permits deduction of those of the parent tertiary amines, relatively high configurational stability being assumed for the latter. In forming the salts (II) and (VI*b*) the quaternising cation must approach the nitrogen atom from the pyrrolidine side of the molecule, which suggests that in each case the acyclic nitrogen substituent initially present is oriented more frequently towards the piperidine ring. Otherwise, quaternisation of the base (I) or (V*b*) should give both *N*-epimers (II) and (VI*b*). Hitherto, however, only the Troeger base, containing two rigidly bound nitrogen atoms, has been resolved (Prelog and Wieland,

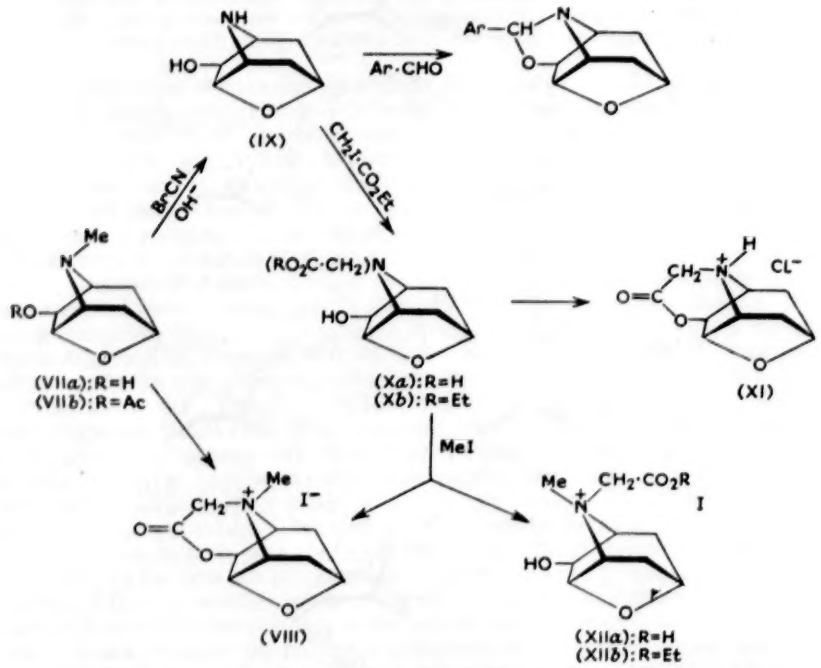


Helv. Chim. Acta, 1944, **27**, 1127; cf. Gilman, "Organic Chemistry," Wiley, 1942, New York, Vol. I, p. 411). Nevertheless, since nitrogen in the tropane system is rigidly bound by two electron pairs, a definite orientation of the third substituent and, according to recent calculations (Lennard-Jones, *Proc. Roy. Soc.*, 1951, *A*, **205**, 357), of the unshared electron pair cannot be excluded.

It remains to explain the more favoured orientation towards the piperidine ring of the acyclic nitrogen substituent in the tertiary bases, especially since this orientation is axial with respect to the six-membered ring. The tropane system might be regarded as a 2 : 6-diaxially substituted piperidine, and since 1 : 3-diaxially substituted *cyclo*hexane rings render a substituent at $C_{(2)}$ more stable when axial than when equatorial (Barton, *Chem. and Ind.*, 1953, 664), the alkyl group at the nitrogen atom would therefore assume an axial position also. However, the selectivity of quaternisation cannot be referred wholly to the piperidine ring, for *N*-alkylpiperidines such as 4-hydroxy-*N*-methylpiperidine (Mills, Parkin, and Ward, *J.*, 1927, 2625), *N*-methylconiine, conhydrine, and even (−)-2-methyl-6-phenylpiperidine (Scholz, *Ber.*, 1904, **37**, 3627) furnish both possible *N*-epimers on

quaternisation. In tertiary amines of the tropane system the *meta*-annelation must cause deformation of the pyrrolidine ring, and consequent operation of the Pitzer effect (*J. Amer. Chem. Soc.*, **1947**, **69**, 2488) will result in a shift of the *N*-methyl group towards the six-membered ring. The configuration of the tertiary nitrogen atom may thus be a factor influencing the ring conformation, for in the chair form the piperidine ring would then avoid repulsion between the *N*-methyl group and the 3-substituent. Further, with tropane-3α : 6β-diol (I) the shift of the *N*-methyl group towards the piperidine ring meets the steric requirement for hydrogen-bonding of the *syn*-hydroxyl group to the unshared electron pair of the nitrogen.

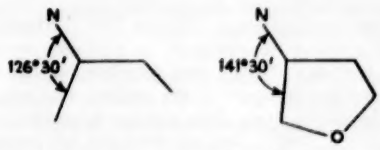
In contrast, the Pitzer effect in the pyrrolidine ring, and the tendency to hydrogen-bonding, are in conflict in other tropane derivatives such as tropan-3β-ol and the ecgonines, where hydrogen-bonding can occur only in the boat form of the piperidine ring.



To estimate the contribution of the deformation in the five-membered ring to the relative configurational stability of nitrogen, oscine (VII*a*) and noroscine (IX) were chosen as models for further " direct " and " reverse " quaternisation experiments. (±)-Oscine acetate (VII*b*) furnished with ethyl iodoacetate the lactone iodide (VIII) in far better yield than does oscine (VII*a*) itself. This may be due to the absence from the acetate (VII*b*) of a hydrogen bond which might hinder quaternisation. (±)-Noroscine (IX), on the other hand, gave with ethyl iodoacetate, (±)-*N*-ethoxycarbonylmethylnoroscine (X*b*), hydrolysis of which was accompanied by spontaneous lactonisation to the hydrochloride (XI). This contrasts with the inability of *N*-carboxymethylnortropane-3α : 6β-diol (V*a*) to lactonise. Further, with methyl iodide the ester (X*b*) gave both the *N*-ethoxycarbonylmethyl derivative (XII*b*) and the lactone of the *N*-epimeric tropanium iodide (VIII). With hydriodic acid the betaine obtained by hydrolysis of the ester salt (XII*b*) afforded the acid (XII*a*) which showed no tendency to cyclise to (VIII). The acid and ester are therefore *Na*-carboxymethyloscinium iodide (XII*a*) and *Na*-ethoxycarbonylmethyloscinium iodide (XII*b*) respectively.

These findings seem to indicate a marked decrease in the configurational stability of the nitrogen atom when $C_{(3)}$ and $C_{(6)}$ in the tropane system are joined by an ether bridge. The bridge draws these carbon atoms towards each other, decreasing simultaneously the deformation of the pyrrolidine ring. Thus, coplanarity is more nearly approached than in the 3 : 6-unbridged skeleton, and the influence of the Pitzer effect in determining the preferred orientation of the acyclic substituent on the nitrogen may be strikingly diminished.

By using values for interatomic distances and unstrained valency angles given in Landolt–Börnstein's tables, scale models of 3α : 6β-dihydroxytropane and oscine have been constructed. In making the projections the interatomic distances were kept unaltered and deformations of the individual valency angles were distributed over the entire molecule. On this basis the angle " α " (see diagram) would be 15° larger in oscine (VII*a*) than in tropane-3α : 6β-diol (I), in accordance with our assumption.



Granatan-3β-ol did not show any appreciable selectivity in quaternisation reactions. Here both rings are flexible (*i.e.*, able to assume chair forms) and no interference of the Pitzer type can be reasonably expected, though this inference needs the support of experimental evidence for the chair form of both rings.

In extension of this work, and in order to establish the limitation of the selectivity, the " direct " and " reverse " quaternisation of tropines with a pseudoasymmetric nitrogen atom, and subsequently of some single pyrrolidines such as γ-hydroxyproline, will be discussed. The curarine-like activity of *N*-epimeric tropanium salts of known *N*-configuration is being investigated by Dr. Gyermek.

Experimental

(*A*) *Derivatives of* (±)-*tropane*-3α : 6β-*diol.*

Direct Quaternisation of (±)-*Tropane*-3α : 6β-*diol* (I).—Ethyl iodoacetate (7·5 ml.) in benzene (50 ml.) was added to (±)-tropane-3α : 6β-diol (5 g.) in dry ethanol (30 ml.), and the mixture refluxed for 14 hr. Filtration and washing with alcohol gave (±)-*Nb*-carboxymethyl-3α : 6β-dihydroxytropanium iodide lactone (III) (4·6 g.), m. p. 263° (decomp.) (Fodor, Tóth, and Vincze, *loc. cit.*), or 259° after crystallisation from alcohol. From alcohol the amorphous residue obtained by evaporating the mother-liquor provided crystals (2·2 g.) which on repeated crystallisation from this solvent gave (±)-Nb-*ethoxycarbonylmethyl*-3α : 6β-*dihydroxytropanium iodide* (II), m. p. 151° (Found : C, 38·5; H, 6·1; I^-, 34·2. $C_{12}H_{22}O_4NI$ requires C, 38·8; H, 6·0; I, 34·2%), which resolidified after melting and remelted at the m. p. of the lactone (III). By refluxing the ester iodide (II) (0·43 g.) in dry alcohol (10 ml.) for 4 hr., evaporating the solution, and recrystallising the residue from dry alcohol, the lactone (III) (0·29 g.), m. p. 258° (decomp.) (Found : C, 37·1; H, 4·8; I, 39·0. Calc. for $C_{10}H_{16}O_3NI$: C, 36·9; H, 5·0; I, 39·0%), was obtained.

Tropane-3α : 6β-*diol Diacetate.*—(±)-Tropane-3α : 6β-diol (I) (19 g.) and acetic anhydride (160 ml.) were refluxed for 3 hr. The solution, in water (20 ml.), of the oil left after removal of acetic anhydride was adjusted to pH 8 with sodium carbonate (0·5 g.), and extracted with chloroform (4 × 100 ml.). Careful evaporation of the dried extract (K_2CO_3) gave tropane-3α : 6β-diol diacetate (25·9 g.) as a viscous oil, $n_D^{22\cdot3}$ 1·4744. This (0·24 g.), in dry ethanol (1 ml.), gave, with a saturated ethanolic solution (9 ml.) of picric acid, yellow crystals of (±)-*tropane*-3α : 6β-*diol diacetate picrate* (0·44 g.), m. p. (unchanged after recrystallisation from ethanol) 174—175° (Found : C, 45·7, 45·8, 45·8; H, 4·5, 4·9, 4·8; N, 11·9. $C_{18}H_{26}O_{11}N_4$ requires C, 45·55; H, 5·5; N, 11·8%).

(±)-N-*Cyanonortropane*-3α : 6β-*diol Diacetate.*—(±)-Tropane-3α : 6β-diol diacetate (25·6 g.) in dry benzene (100 ml.) was stirred at 65—70° and treated dropwise during 1 hr. with *carefully dried* cyanogen bromide (20 g.) in benzene (100 ml.). After a further 3 hours' stirring at the

same temperature the white crystalline salt (4·7 g.), m. p. 258° (decomp.), was collected, washed with a little benzene, and recrystallised from dry ethanol (35 ml.) to give (±)-N-*methyl*-3α : 6β-*diacetoxytropanium bromide* (3·55 g.), m. p. 275° (Found : C, 46·8; H, 7·4; N, 4·4; Br^-, 23·4. $C_{13}H_{22}O_4NBr$ requires C, 46·4; H, 6·6; N, 4·2; Br, 23·7%).

The oil obtained by evaporating the reaction mixture under reduced pressure readily crystallised and was collected (22·3 g.; m. p. 111°) with the help of ether. Crystallisation from ethyl acetate–benzene gave the N-*cyano-compound*, m. p. 112—113° (Found : C, 56·8; H, 6·4; N, 11·0. $C_{12}H_{16}O_4N_2$ requires C, 57·1; H, 6·4; N, 11·1%).

(±)-*Nortropane*-3α : 6β-*diol*.—The *N*-cyano-compound (21 g.) and aqueous sodium hydroxide (10%; 210 ml.) were stirred for 12 hr. on the steam-bath. The dried ($MgSO_4$) butanol (3 × 50 ml.) extract of the cooled mixture gave on evaporation a coloured crystalline product (6·7 g.; m. p. 180°). This gave (±)-*nortropane*-3α : 6β-*diol*, m. p. 203—204° (Found : C, 58·6; H, 9·1; N, 9·5. $C_7H_{13}O_2N$ requires C, 58·7; H, 9·2; N, 9·8%), on crystallisation from dry ethanol.

(±)-Na-*Ethoxycarbonylmethylnortropane*-3α : 6β-*diol* (Vb).—Ethyl iodoacetate (0·54 ml.) in benzene (2 ml.) was added at room temperature to (±)-nortropane-3α : 6β-diol (1·3 g.) in anhydrous alcohol (6 ml.), benzene (7 ml.), and nitrobenzene (7 ml.). Some crystals soon appeared and after 2 days the greater part of the solvent was removed at reduced pressure, below 50°. With alcohol the partly crystalline residue furnished (±)-nortropane-3α : 6β-diol hydriodide (1·09 g., 89%), m. p. 220°. The oil obtained by evaporating the mother-liquor below 50° was treated, under cooling, with anhydrous 4N-ethanolic hydrogen chloride (5 ml.). Addition of dry ether (40 ml.) precipitated an oil which formed a white powder (1·37 g., 86%) when rubbed. Recrystallisation from dry ethanol gave Na-*ethoxycarbonylmethylnortropane*-3α : 6β-*diol hydrochloride*, m. p. 175—176° (decomp.) (Found : C, 49·4; H, 7·4; N, 5·3; Cl, 13·4. $C_{11}H_{20}O_4NCl$ requires C, 49·7; H, 7·4; N, 5·3; Cl, 13·3%).

From a similar experiment we isolated the free base. Nortropane-3α : 6β-diol in dry alcohol (10·5 ml.), dry benzene (7·5 ml.), and nitrobenzene (7·5 ml.) was treated with freshly distilled ethyl iodoacetate (0·9 ml.) in nitrobenzene (2 ml.). After 1 day at room temperature nortropane-3α : 6β-diol hydriodide (90%) separated, and from the mother-liquor, the product (1·2 g.; m. p. 104—106°). Recrystallisation from alcohol gave (±)-Na-*ethoxycarbonylmethylnortropane*-3α : 6β-*diol*, m. p. 106—107° (Found : C, 57·7; H, 8·7; N, 6·0. $C_{11}H_{19}O_4N$ requires C, 57·6; H, 8·4; N, 6·1%).

(±)-Na-*Carboxymethylnortropane*-3α : 6β-*diol Hydrochloride*.—The solution formed by heating the above ester hydrochloride (0·4 g.) and hydrochloric acid (5 ml.) for 5 hr. on the steam-bath was evaporated to dryness. Water (2 × 5 ml.) was added to the residue and removed under reduced pressure. Crystallisation of the foamy product from alcohol–ether (1 : 4, 5 ml.) gave the *carboxylic acid hydrochloride* (0·22 g., 62%), m. p. 190° (decomp.) (Found : C, 45·3; H, 6·9; N, 5·8; Cl, 15·0. $C_9H_{16}O_4NCl$ requires C, 45·5; H, 6·8; N, 5·9; Cl, 14·9%).

Na-*Ethoxycarbonylmethyl*-3α : 6β-*dihydroxytropanium Iodide* (VIb).—(i) (±)-Nortropane-3α : 6β-diol (1·43 g.) was treated with ethyl iodoacetate as above. Alcohol and benzene were removed below 40°, and nortropane-3α : 6β-diol hydriodide (1·0 g., 73%) was collected from the residue. The remaining nitrobenzene solution was treated with methyl iodide (8 g.) and set aside in darkness. Crystallisation soon began and after 2 days the product (1·15 g.; m. p. 193°) was collected. Recrystallisation from ethanol gave (±)-Na-*ethoxycarbonylmethyl*-3α : 6β-*dihydroxytropanium iodide*, m. p. 194° (Found : C, 39·1; H, 6·6; N, 4·0; I^-, 34·2. $C_{13}H_{22}O_4NI$ requires C, 38·8; H, 6·0; N, 3·8; I′, 34·2%).

(ii) Sodium ethoxide solution (4·86%; 0·71 ml.) was added to (±)-*Na*-ethoxycarbonylmethylnortropane-3α : 6β-diol hydrochloride (0·4 g.) in dry ethanol (3 ml.). After centrifuging, the separated sodium chloride (0·105 g.; theor. 0·086 g.) was washed with benzene (3·5 ml.), and the combined alcoholic and benzene solutions were treated with methyl iodide. In 10 hr. crystals had separated, and after 3 days filtration isolated a product (0·37 g.), m. p. 194° (decomp.), identical with that above. Evaporation of the mother-liquor and treatment with acetone gave a further crop (0·08 g.), m. p. 150—160°.

(±)-Na-*Carboxymethyltropane*-3α : 6β-*diol Betaine*.—(±)-*Na*-Ethoxycarbonylmethyl-3α : 6β-dihydroxytropanium iodide (0·35 g.), water (8 ml.), and silver oxide (0·18 g.) were shaken together for 4 hr. After filtration the solution was evaporated *in vacuo*. The solution of the residue in alcohol (20 ml.) was filtered and repeatedly evaporated. The *betaine* (0·18 g., 90%), m. p. 270° (decomp.) (Found : C, 55·8; H, 8·3; N, 6·3. $C_{10}H_{17}O_4N$ requires C, 55·8; H, 8·0; N, 6·5%), crystallised from dry ethanol.

(±)-Na-*Carboxymethyl*-3α : 6β-*dihydroxytropanium Iodide*.—The betaine (0·4 g.) solution in

concentrated hydriodic acid was evaporated to dryness. Crystallisation of the residue from dry ethanol (3 ml.) gave the *iodide* (0·44 g.), m. p. 202° (decomp.) (Found : C, 35·2; H, 6·1; N, 4·1; I^-, 36·9. $C_{10}H_{18}O_4NI$ requires C, 35·0; H, 5·3; N, 4·1; I, 37·0%).

(*B*) *Derivatives of* (±)-*oscine.*

(±)-*Oscine Acetate.*—(±)-Oscine (3·1 g.), benzene (20 ml.), and acetyl chloride (30 ml.) were kept for 3 hr. at 75°. (±)-*Oscine acetate hydrochloride* (3·3 g., 80·5%), m. p. 199—201° (Found : C, 51·6; H, 6·8; N, 6·2; Cl^-, 15·4. $C_{10}H_{18}O_2NCl$ requires C, 51·4; H, 6·9; N, 6·0; Cl, 15·3%), was collected and washed with acetone. The dried (Na_2CO_3) chloroform (9 × 10 ml.) extract of a basified (to pH 8 with sodium carbonate) solution of this salt (2·7 g.) in water (10 ml.) gave an oily base (2·2 g., 96%) on evaporation.

(±)-Nb-*Carboxymethyloscinium Iodide Lactone* (VIII).—When (±)-oscine acetate (2·5 g.), benzene (2 ml.), and ethyl iodoacetate (3 ml.) were kept for 1 day a viscous oil separated. Triturated with acetone, this gave a solid which from alcohol afforded crystals (2·35 g., 81%), m. p. 246° (decomp.), of the lactone previously described (Fodor, Tóth, and Vincze, *Helv. Chim. Acta*, 1954, **37**, 907).

(±)-N-*Cyanonoroscine Acetate.*—(±)-Oscine acetate (15·8 g.) in dry benzene (60 ml.) was added during 1·5 hr. to cyanogen bromide (17 g.), stirred in dry benzene (80 ml.) at 60—70°. The mixture was kept for 3 hr. more at this temperature and a solid [0·58 g.; m. p. 261° (decomp.), resembling a quaternary salt] removed. Evaporated *in vacuo*, the filtrate provided yellow crystals (14·3 g.; m. p. 83—85°) which by crystallisation from dry alcohol gave the product (10·7 g.), m. p. 90—91°. Further crystallisation gave pure (±)-N-*cyanonoroscine acetate*, m. p. 91° (Found : C, 58·0; H, 6·2; N, 13·4. $C_{10}H_{12}O_2N_2$ requires C, 57·7; H, 5·8; N, 13·4%).

(±)-*Noroscine.*—The suspension of the cyano-compound (9·7 g.) in aqueous sodium hydroxide (10%; 100 ml.) was kept at 100° for 12 hr. The chloroform extract of the residue obtained by evaporating the solution below 50° *in vacuo* was evaporated. Addition of light petroleum gave a product (5·34 g.), m. p. 190—195°, which on crystallisation from chloroform–light petroleum provided (±)-noroscine (4·82 g.), m. p. 204—205°, identical with a sample obtained by permanganate oxidation of oscine (Hess, Merck, and Uibrig, *Ber.*, 1915, **48**, 1889, 1906).

" *Reverse Quaternisation* " *of* (±)-*Noroscine.*—(±)-Noroscine (2·82 g.) in dry ethanol (5 ml.) and dry benzene (10 ml.) was treated with nitrobenzene (10 ml.) and ethyl iodoacetate (2·14 g.). Crystals soon separated, and after 12 hr. (±)-noroscine hydriodide (2·42 g.), m. p. 298° (decomp.) (Found : I, 46·9. $C_7H_{12}O_2NI$ requires I, 47·2%), was collected. Methyl iodide (10 ml.) was added to the filtrate and after 2 days needles of (±)-*Nb*-carboxymethyloscinium iodide lactone (0·42 g.), m. p. 246° (decomp.) (Fodor *et al.*, *loc. cit.*) were obtained. Evaporation of the filtrate under reduced pressure gave an amorphous residue, which from alcohol (3 ml.) gave after 1 day in the refrigerator a product [0·34 g.; m. p. 175° (decomp.)]. Recrystallisation from the same solvent (6 ml.) gave (±)-Na-*ethoxycarbonylmethyloscinium iodide* (0·23 g.), m. p. 181° (decomp.) (Found : C, 39·2; H, 5·6; N, 3·6; I, 34·1. $C_{12}H_{20}O_4NI$ requires C, 39·0; H, 5·5; N, 3·8; I, 34·4%).

(±)-Na-*Carboxymethyloscine Betaine.*—The above ester iodide (0·37 g.), water (8 ml.) and silver oxide (0·18 g.) were shaken for 6 hr. Filtration, evaporation to dryness, and crystallisation of the resulting mixture of crystals and foam from dry ethanol gave the *betaine*, m. p. 295° (decomp.) (Found : C, 56·3; H, 7·3; N, 6·8. $C_{10}H_{15}O_4N$ requires C, 56·3; H, 7·1; N, 6·6%).

(±)-Na-*Carboxymethyloscinium Iodide.*—The residue obtained by evaporating the betaine (0·11 g.) and freshly distilled hydriodic acid (4 ml.) *in vacuo* on the steam-bath was dissolved in anhydrous ethanol (3 × 5 ml.) and again evaporated. Crystallisation of the product from dry ethanol (2 ml.) gave (±)-Na-*carboxymethyloscinium iodide* (0·09 g.), m. p. 179° (decomp.) (Found : C, 35·2; H, 5·2; N, 4·2; I, 36·6. $C_{10}H_{16}O_4NI$ requires C, 35·2; H, 4·7; N, 4·1; I, 37·1%).

(±)-N-*Ethoxycarbonylmethylnoroscine Hydrochloride.*—(±)-Noroscine (3·94 g.) was treated with ethyl iodoacetate (3 g.) in nitrobenzene, alcohol and benzene. Noroscine hydriodide was removed in nearly theoretical yield and the filtrate was treated with a 20% solution (6 ml.) of hydrogen chloride in dioxan, and with ether (100 ml.). Trituration of the precipitate gave a crystalline powder [3·7 g.; m. p. 198° (decomp.)] which on crystallisation from dry alcohol afforded (±)-N-*ethoxycarbonylmethylnoroscine hydrochloride* (2·51 g.), m. p. 205° (decomp.) (Found : C, 50·3; H, 6·3; N, 5·3; Cl^-, 13·6. $C_{11}H_{18}O_4NCl$ requires C, 50·1; H, 6·8; N, 5·3; Cl, 13·4%).

(±)-Nb-*Carboxymethylnoroscine Lactone Hydrochloride.*—The above hydrochloride (1·16 g.) was thrice evaporated to dryness *in vacuo* with concentrated hydrochloric acid (10 ml.). Trituration of the glass-like residue with acetone and recrystallisation of the filtered product

[0·95 g.; m. p. 275° (decomp.)] from dry ethanol gave the *lactone*, m. p. 276° (decomp.) (Found: C, 49·5; H, 5·7; N, 6·4; Cl^-, 16·3. $C_9H_{12}O_3NCl$ requires C, 49·7; H, 5·6; N, 6·6; Cl, 16·3%).

Quaternisation of N-Ethoxycarbonylmethylnoroscine.—(±)-*N*-Ethoxycarbonylmethylnoroscine hydrochloride (1·3 g.), when treated with ethanolic sodium ethoxide (2·17%; 5·25 ml.) in dry ethanol (10 ml.) and with methyl iodide (5 ml.), gave (±)-*Na*-ethoxycarbonylmethyloscinium iodide (0·10 g.) and (±)-*Nb*-carboxymethyloscinium iodide lactone (0·80 g.).

Oxazines from (±)-Noroscine.—Solvent was distilled from a solution of (±)-noroscine (0·7 g.), *p*-nitrobenzaldehyde (0·75 g.), and chlorobenzene (50 ml.). This process was repeated three times (no more water was then formed), and the mixture was evaporated to dryness. Recrystallisation of the residue (1·35 g.; m. p. 178—179°) from dry benzene gave the oxazine (1·1 g.), m. p. 183° (Heusner *et al.*, *Chem. Ber.*, 1954, **87**, 1063, give m. p. 183°).

Similarly, (±)-noroscine (0·7 g.) and piperonaldehyde (0·75 g.) gave a product which on crystallisation from benzene gave the *oxazine* (0·55 g.), m. p. 145—146° (Found: C, 65·9; H, 5·5; N, 5·2. $C_{15}H_{15}O_4N$ requires C, 65·9; H, 5·5; N, 5·1%).

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Lipids. Part III. Determination of Hydrogenation Selectivity in the Synthesis of* cis*-Fatty Acids.*

By L. Crombie.

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Reversed-phase partition chromatography is suitable for the analysis of mixtures of acetylenic, ethylenic, and saturated acids encountered in the synthesis of *cis*-long-chain fatty acids by catalytic semihydrogenation. Selectivity of four catalysts for production of undec-10-enoic acid from undec-10-ynoic acid is examined.

At the present time, the most important synthetical process for introducing a *cis*-ethenoid linkage is catalysed semihydrogenation of the corresponding acetylene. The process suffers from two major drawbacks. First, the reaction is not fully stereospecific (*i.e.*, small amounts of *trans*-isomer are also formed) and, secondly, it is not completely selective (*i.e.*, some olefin is saturated before all the acetylene has disappeared). Analytical methods using infrared or Raman techniques are suitable for determination of *trans*- in the presence of *cis*-material (cf. Shreve, Heather, Knight, and Swern, *Analyt. Chem.*, 1950, **22**, 1261). Selectivity is less easily estimated by infrared methods: because of the lack of suitable vibrations it is often difficult to determine small amounts of acetylenic or saturated acids when much olefinic acid is present. Partition chromatography is now applied to the estimation of acetylenic, ethylenic, and saturated long-chain fatty acids in mixtures.

Howard and Martin's reversed-phase technique (*Biochem. J.*, 1950, **46**, 532; Popják and Tietz, *ibid.*, 1954, **56**, 46; Silk and Hahn, *ibid.*, p. 406), which employs a column of paraffin supported on silane-treated kieselguhr with acetone–water mixtures as eluant, has recently been applied to the separation of a wide range of plant fatty acids (W. Mary L. Crombie, Comber, and Boatman, *ibid.*, 1955, **59**, 309). It is also suitable for the present purpose. Test mixtures such as might be encountered in synthesis of oleic, petroselinic, and undec-10-enoic acids by semihydrogenation were found to be separable, and analyses are summarised in Table I. It is likely that the method is applicable to acids of chain lengths C_{10}—C_{24} with unsaturation at most points along the chain except $C_{(2)}$. The presence of a little *trans*-impurity in the *cis*-fatty acid causes no difficulty as resolution of the two stereoisomers is incomplete and they appear as one band.

To illustrate the capabilities of the method a few catalytic hydrogenation products

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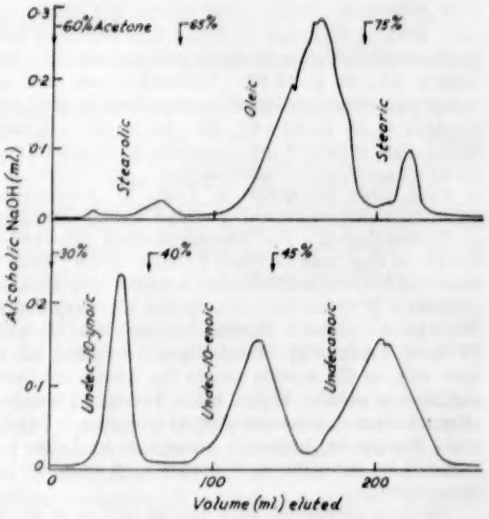
from undec-10-ynoic acid have been examined. In this work correlation between measured hydrogen uptake and product analysis is not quantitative. The products appear to have been hydrogenated rather more than the burette readings indicate and this probably

TABLE 1. *Analysis of mixtures of acetylenic, olefinic, and saturated long-chain acids.*

Acid	Composition (%)	Found (%)	Acid	Composition (%)	Found (%)
Stearolic	5·4	3·7	Tariric	1·6	1·2
Oleic	85·1	86·7	Petroselinic	95·4	95·5
Stearic	9·5	9·6	Stearic	3·0	3·2
Undec-10-ynoic	6·2	6·0	Tariric	2·9	3·4
Undec-10-enoic	85·4	86·1	Petroselinic	88·1	86·3
Undecanoic	8·4	7·9	Stearic	9·0	10·5

reflects inability to apply adequate corrections with the standard laboratory equipment used : furthermore the system cannot be allowed to come to equilibrium if hydrogenation must be interrupted at a certain level. Hydrogen volumes absorbed must therefore be accepted as approximate and are recorded to the nearest 5%.



Upper curve : Separation of test mixture (see Table 1).

The unmarked first peak is due to a trace of autoxidised material in the oleic acid.

Lower curve : Separation of products from partial hydrogenation of undec-10-ynoic acid with Adams's catalyst (see Table 2).

The arrows indicate points at which the concentration of the eluting solvent (acetone–water) was changed. Successive effluent volumes of 2 ml. were titrated.

The gross unselectivity of Adams's platinum catalyst is shown in the Figure (see also Table 2). Even when 1·2 mol. of hydrogen have been absorbed there is still a large residue of unchanged acetylenic acid : it is unsuitable for synthetical work. Raney nickel (W4) has also given poor results in the present case. Palladium on barium sulphate has much higher selectivity, but Table 2 shows that after approximately one mol. of hydrogen has

TABLE 2. *Hydrogenation of undec-10-ynoic acid.*

Catalyst	Solvent	Measd. H_2 absorption (mol.)	·C:CH (%)	·CH:CH_2 (%)	·CH_2·CH_3 (%)
Adams platinum	EtOAc	1·15	21·5	35·5	43
Raney nickel (W4)	Pet [b]	0·85	32·0	36·0	32
Palladium–barium sulphate	EtOAc	1·2	Nil	67	33
" " "	"	1·0	4·5	87	8·5
Lindlar Pb–Pd–$CaCO_3$ [a]	"	1·05 [c]	Nil	91	9·0
" "	Pet [b]	1·1 [c, d]	Nil	91·5	8·5
" "	"	1·0 [d]	Nil	94·5	5·5
" "	"	0·85 [d]	9·0	88·0	3·5

[a] Poisoned with quinoline in the usual way. [b] Light petroleum (b. p. 80—100°), treated with Raney nickel before use. [c] Absorption ceased spontaneously. [d] Experiments on a macroscale.

been absorbed 8·5% of saturated impurity is present even though a little acetylenic material remains unchanged.

If undec-10-ynoic acid is hydrogenated with quinoline-poisoned lead–palladium–calcium carbonate (Lindlar, *Helv. Chim. Acta*, 1952, **35**, 446) in ethyl acetate, absorption of gas ceases when rather more than one mol. has been used. At this stage no acetylenic acid remains but 9% of undecanoic acid is present. The same result was obtained in light petroleum, with a much smaller amount of catalyst. By interruption of the reaction a little before hydrogenation ceases spontaneously, the quantity of saturated acid is reduced but even when 9% of acetylenic acid remains unhydrogenated small amounts of saturated acid have been formed. Despite the inconvenience of removing quinoline from the product, Lindlar's system is the best catalyst for this semireduction and the slowing of gas absorption near uptake of one mol. facilitates manipulation. Dr. B. C. L. Weedon has allowed the author to examine a specimen of stearolic acid hydrogenated with Lindlar catalyst until absorption ceased. This contained no acetylenic acid and less than 2% of stearic acid, so selectivity seems almost complete in this case which involves an internal triple linkage.

Experimental

Materials.—Undec-10-enoic acid (commercial) was purified to m. p. 25—25·5° by fractional melting (lit., m. p. 24·5°). Undec-10-ynoic acid, prepared by A. G. Jacklin by bromination and dehydrobromination of undec-10-enoic acid, was crystallised from light petroleum (b. p. 60—80°) to m. p. 43—44° (lit., m. p. 43°). Undecanoic acid, m. p. 28·5—29·0° (lit., m. p. 28·5°), was prepared by complete hydrogenation of undec-10-ynoic acid. The acids were chromatographically homogeneous. The author is grateful to Dr. B. C. L. Weedon for gifts of some acids mentioned in Table 1. Petroselinic acid, from a natural source, contained impurity which was speedily eluted during chromatography: a correction was made for this.

Hydrogenation.—For semimicro-work (30—100 mg.) an apparatus with magnetic stirring similar to Ogg and Cooper's (*Analyt. Chem.*, 1949, **21**, 1400) was used. The solvent volume was 5 ml. Catalysts: Adams catalyst was from a commercial source (Johnson & Matthey); palladium (5%) on barium sulphate was prepared according to Houben ("Die Methoden der Organische Chemie," Thieme, Leipzig, Vol. II, p. 500), and Raney nickel (W4) according to Pavlic and Adkins (*J. Amer. Chem. Soc.*, 1946, **68**, 1471) and aged for 4 weeks. Amounts used were 10% of the sample weight for Adams catalyst, and 25% for palladium–barium sulphate and Raney nickel. With Lindlar catalyst a weight equal to that of the sample was employed after addition of a minute drop of quinoline. Catalysts were equilibrated with hydrogen before use. Figures for hydrogen absorption in Table 1 are calculated on the volume of hydrogen required for complete hydrogenation of undec-10-ynoic acid to undecanoic acid as determined experimentally.

Macro-experiments were carried out in a small standard laboratory hydrogenator, with mechanical shaking. Samples were approx. 500 mg. In experiments with light petroleum (5 ml.; b. p. 80—100°) the weight of Lindlar catalyst was 10% of the sample weight and the quinoline added was 40% of the catalyst weight. Semi-reduction was achieved in about 30 min.

Chromatography.—The technique was essentially as described by Howard and Martin (*loc. cit.*). In a few cases, where the amount of saturated acid was low, its presence was confirmed by Bertram oxidation (which converts unsaturated compounds into acids which are eluted speedily), followed by chromatography (W. Mary L. Crombie, Comber, and Boatman, *loc. cit.*). As the oxidation conditions cause loss of some undecanoic acid this provides only a qualitative check.

The possibility of employing infrared spectroscopy for analysis of mixtures of undec-10-enoic acid containing small amounts of undec-10-ynoic and undecanoic acids was examined. No reliable estimate of small quantities of saturated acid was possible, though because of the terminal position of the acetylenic linkage an approximate figure for undec-10-ynoic acid could be obtained by use of the C≡C–H stretching frequency.

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The Diamagnetic Susceptibilities of Some Oximes and Oxime Ethers.

By C. M. French and D. Harrison.

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The diamagnetic susceptibilities of six oximes of various structural types and four oxime ethers have been measured by the Gouy method. The values obtained are in poor agreement with those calculated by Pascal's method, nor can they be satisfactorily interpreted on the basis of the recent " Modified Bond Additivity System " (French and Harrison, *J.*, 1955, 1990). It is suggested that the origin of the divergences lies in interactions between groups attached to the C:N bond, an effect analogous to that postulated by Lacher, Pollock, Johnson, and Park (*J. Amer. Chem. Soc.*, 1951, **73**, 2838) in methyl-substituted ethylenes. Other factors which may influence the susceptibilities of oximes and oxime ethers are briefly discussed.

Diamagnetic susceptibilities of many compounds containing only carbon, hydrogen, and oxygen have recently been investigated, but since the early work of Pascal (*e.g.*, *Bull. Soc. chim. France*, 1911, **9**, 336) little attention has been paid to simple compounds containing also nitrogen.

In building up his system of additive and constitutive constants, Pascal found more difficulty with compounds containing nitrogen than with those formed from carbon, hydrogen, and oxygen only, especially with compounds with functional groups containing both oxygen and nitrogen, such as oximes and oxime ethers. In Pascal's method of calculation, correction terms for tertiary and quaternary carbon atoms near functional groups containing oxygen are included, and in order to apply these terms to compounds containing nitrogen and oxygen Pascal assumed that a system such as >C:N·O· could be treated as equivalent to >C:CMe·O, the same correction terms being applicable in each case. This rather extraordinary procedure was supported in the case of oximes by measurements on four compounds only, two of which had by no means simple structures; Pacault (*Rev. sci.*, 1948, **86**, 38), reviewing Pascal's method, adopted this procedure without comment or modification.

It seemed of interest to measure the susceptibilities of some simple oximes and oxime ethers in order to test the validity of Pascal's method of calculation in such compounds. Oxime ethers were included because, although tautomerism in simple oximes is now regarded as highly improbable, it cannot be ruled out (cf. Dunitz and Robertson, *Ann. Reports*, 1952, **49**, 378). Susceptibilities of the parent carbonyl compounds were also measured, in order to evaluate the susceptibility increment for the transition >C:O → >C:N·OH.

Experimental

Materials.—Benzene (B.D.H. extra pure for molecular-weight determinations) was shaken three times with concentrated sulphuric acid, washed with distilled water, and dried ($CaCl_2$) for 3 days. It was then fractionally frozen three times (the last third to freeze being rejected each time), dried (P_2O_5), and carefully fractionated at 1 atm., all but the middle third of the distillate being rejected, through a column packed with Fenske helices (efficiency approximately 15 theoretical plates), which was also used for the fractionation of the ketones and oximes.

Acetone (" AnalaR ") was refluxed with alkaline potassium permanganate for 6 hr., filtered, dried (K_2CO_3) for 1 week, and then twice fractionated, with rejection of all but the middle third in each case. Ethyl methyl ketone, diethyl ketone, and *n*-hexyl methyl ketone were dried (K_2CO_3) and purified by repeated fractionation. *n*-Hexyl methyl ketone was fractionated under reduced pressure, since there were signs of decomposition at atmospheric pressure. As a check, small amounts of these ketones were also purified *via* the semicarbazone (Cowan, Jeffery, and Vogel, *J.*, 1940, 171).

Acetophenone was dried for 3 days ($CaCl_2$) and then purified by fractional freezing, as described by Morgan and Lammert (*J. Amer. Chem. Soc.*, 1924, **46**, 881), followed by fractional

distillation (15 mm.). *iso*Butyraldehyde was dried (Na_2SO_4) and repeatedly fractionated at atmospheric pressure. It was found essential to use the aldehyde immediately after purification, because of the great difficulty in preventing oxidation. *cyclo*Hexanone, after preliminary fractionation at atmospheric pressure, was purified *via* the bisulphite compound (Vogel, " A Text-book of Practical Organic Chemistry," Longmans, London, 1948, p. 340) and finally fractionated (20 mm.).

The oximes were prepared from the carbonyl compounds and hydroxylamine hydrochloride by standard methods. The solid oximes (*i.e.*, of acetone, *cyclo*hexanone, and acetophenone) were purified by repeated recrystallisation from " AnalaR " light petroleum (b. p. 60—80°), and the liquids by fractional distillation under reduced pressure.

Acetoxime *O*-methyl ether was prepared by Ponzio and Charrier's method (*Gazzetta*, 1907, **37**, 506). The best yields were obtained by cooling the mixture in ice and separating the product from the aqueous residue as soon as possible after reaction had ceased.

Acetophenone oxime *O*-methyl ether was obtained by a modification of Dunstan and Goulding's method (*J.*, 1901, **79**, 628). Dry acetophenone oxime (40 g.) was dissolved in a solution of sodium (7 g.) in dry ethanol (150 ml.). Methyl iodide (43 g.) was added in small portions and the mixture refluxed gently for 5 hr. Most of the ethanol was distilled off, and the residue poured into cold water. Ether was added, the ethereal layer was separated and dried ($CaSO_4$), and the ether removed. The residue was distilled at 12 mm. The middle fraction (b. p. 91—92°) was acetophenone oxime *O*-methyl ether (19·6 g.) (Found : C, 72·7; H, 7·4; N, 9·2. Calc. for $C_9H_{11}ON$: C, 72·5; H, 7·4; N, 9·4%). The product was redistilled twice before use.

*cyclo*Hexanone oxime *O*-methyl ether was prepared by Hudlicky and Hockr's method (*Coll. Czech. Chem. Comm.*, 1949, **14**, 561). Although acetoxime *O*-benzyl ether was prepared by Janny (*Ber.*, 1883, **16**, 174) it does not appear to have been previously obtained *pure*. Sodium (6·3 g.) was dissolved in absolute ethanol (150 ml.), and to the solution were added in turn dry acetoxime (20 g.) and redistilled benzyl chloride (31 ml.). The mixture was gently refluxed for 2 hr. When cool, it was poured into ice-cold water (250 ml.), and the oil extracted with ether (2 × 100 ml.). The extract was washed with small portions of water and dried ($CaSO_4$), and the ether was distilled off. The residue was fractionally distilled (1·5 mm.), the acetoxime *O*-benzyl ether being obtained as a fraction, b. p. 65—66° (20 g.) (Found : C, 73·5; H, 8·1; N, 8·7. Calc. for $C_{10}H_{13}ON$: C, 73·6; H, 8·0; N, 8·6).

The identity of the oxime ethers was confirmed by hydrolysis with 20% hydrochloric acid, and isolation of the corresponding substituted hydroxylamine hydrochloride and ketone. The boiling (or melting) points, densities, and refractive indices of all the compounds studied are recorded in Table 1.

TABLE 1.

		RR'CO			RR'C:NOH		
R	R'	B. p./mm.	n_D^{20}	d_4^{20}	B. p./mm.	n_D^{20}	d_4^{20}
Me	Me	56·0°/755	1·3591	0·7903	(m. p. 59—60°)	—	1·05
Et	Me	79·4—79·6/760	1·3785	0·8054	71·5—72/26	1·4427	0·9238
Et	Et	101·5—102/763	1·3925	0·8143	75—75·5/15	1·4463	0·9139
n-Hexyl	Me	75·5/24	1·4156	0·8185	121—122/20	1·4515	0·8852
Ph	Me	87—88/15	1·5341	1·0279	(m. p. 59—60)	—	1·17
Pr^i	H	64/760	1·3733	0·7931	51/15	1·4301	0·8949
RR' =	$<[CH_2]_5$	51—52/20	1·4501	0·9478	(m. p. 87—88)	—	1·01

		RR'C:N·OMe			RR'C:N·O·CH_2Ph		
Me	Me	72·5—73/763	1·3997	0·8331	65—66/1·5	1·5137	0·9852
Ph	Me	58—59/15	1·4656	0·9472	—	—	—

Physical Measurements.—Magnetic susceptibilities were measured by the Gouy method. The magnet was a copy of that described by Bates and Lloyd Evans (*Proc. Phys. Soc.*, 1933, **45**, 425), with a pole gap of 17 mm. and exciting current of 12·5 A producing a field of 12,750 gauss at the centre of the pole gap. It was calibrated with pure benzene ($\chi = -0{\cdot}702 \times 10^{-6}$ e.m.u. g.$^{-1}$). With solids, great care was taken to ensure uniformity of packing, and the formula given by French and Harrison (*J.*, 1953, 2338) was used. The standard deviation of the χ value was calculated in each case, although it is not certain that application of such statistical methods to susceptibility measurements (in which errors are often of a

systematic nature) is justified. The standard deviations were roughly $0{\cdot}001 \times 10^{-6}$ for liquids and $0{\cdot}004 \times 10^{-6}$ for solids.

Refractive indices for the sodium-D line were measured at 20·0° ± 0·05° with a Bellingham and Stanley critical-angle refractometer. Densities of liquids were measured, at 20·0° ± 0·02°, in a 5 c.c. density bottle with tightly-fitting cap. Densities of powdered solids were measured in the same density bottle, with either conductivity water or light petroleum (b. p. 60—80°) as filling liquid.

In Table 2 the experimentally determined values of the specific susceptibility (χ) and the molar susceptibility (χ_m) are recorded. For some ketones agreement with other recently recorded values is less good than expected. We believe this to be due partly to the difficulty of purifying these compounds. For this reason, the methods of purification and physical constants of the materials used have been given in full. We advise that this practice should be generally adopted, so that at least some discrepancies in recorded susceptibility values could be explained.

TABLE 2.

Compound	$-10^6\chi$	$-10^6\chi_m$	Other recorded values
Acetone	$0{\cdot}581_1$	$33{\cdot}7_2$	24 values—see ref. 1
Ethyl methyl ketone	$0{\cdot}632_3$	$45{\cdot}5_9$	45·60 [2]; 47·74 [3]; 46·97 [4]; 45·86 [5]; 45·60 [1]
Diethyl ketone	$0{\cdot}675_1$	$58{\cdot}1_4$	58·31 [5]; 57·32 [1]
n-Hexyl methyl ketone	$0{\cdot}713_1$	$91{\cdot}4_3$	91·6 [6]; 93·31 [2]; 92·07 [1]
Acetophenone	$0{\cdot}603_5$	$72{\cdot}5_0$	72·38 [3]; 72·05 [7]; 72·2 [8]; 72·05 [9]
*iso*Butyraldehyde	$0{\cdot}655_9$	$47{\cdot}2_9$	46·2 [6]; 45·6 [10]; 47·45 [3]; 46·38 [1]
*cyclo*Hexanone	$0{\cdot}632_3$	$62{\cdot}0_4$	63·46 [11]; 61·98 [12]
Acetoxime	$0{\cdot}607_6$	$44{\cdot}4_2$	—
Ethyl methyl ketoxime	$0{\cdot}658_0$	$57{\cdot}3_2$	—
Diethyl ketoxime	$0{\cdot}675_4$	$68{\cdot}3_1$	—
n-Hexyl methyl ketoxime	$0{\cdot}716_3$	$102{\cdot}5_8$	102·43 [13]
Acetophenone oxime	$0{\cdot}592_0$	$79{\cdot}9_0$	—
*iso*Butyraldoxime	$0{\cdot}644_3$	$56{\cdot}1_3$	55·87 [13]
*cyclo*Hexanone oxime	$0{\cdot}632_1$	$71{\cdot}5_2$	—
Acetoxime *O*-methyl ether	$0{\cdot}629_8$	$54{\cdot}8_7$	—
Acetophenone oxime *O*-methyl ether	$0{\cdot}618_8$	$92{\cdot}3_1$	—
*cyclo*Hexanone oxime *O*-methyl ether	$0{\cdot}652_3$	$82{\cdot}9_6$	—
Acetoxime *O*-benzyl ether	$0{\cdot}642_7$	$104{\cdot}8_9$	—

Refs. :—[1] Angus, Llewelyn, and Stott, *Trans. Faraday Soc.*, 1955, **51**, 241. [2] Pascal, *Bull. Soc. chim. France*, 1911, **9**, 177. [3] Bhatnagar and Dhawan, *Phil. Mag.*, 1928, **5**, 536. [4] Cabrera and Madinaveitia, *Anales Fis. Quim.*, 1932, **30**, 528. [5] Seguin, *Compt. rend.*, 1947, **224**, 928. [6] Henrichsen, *Ann. Phys.*, 1888, **34**, 180. [7] Angus, *Bull. Soc. chim. France*, 1949, **16***D*, 483. [8] Cherrier, *Compt. rend.*, 1948, **226**, 1016. [9] Angus and Llewelyn, *Trans. Faraday Soc.*, 1955, **51**, 245. [10] Pascal, *Compt. rend.*, 1909, **149**, 343. [11] Pascal, *Bull. soc. chim. France*, 1911, **9**, 809. [12] Farquharson and Sastri, *Trans. Faraday Soc.*, 1937, **33**, 1474. [13] Pascal, *Bull. Soc. chim. France*, 1911, **9**, 336.

DISCUSSION

Susceptibility values calculated by Pascal's method, using Pacault's revised constants (*loc. cit.*), often differ considerably from our experimental values, even for ketones. A few of the more serious divergences are given in Table 3.

TABLE 3.

Compound	χ_m (exp.)	χ_m (calc.) Pascal	Compound	χ_m (exp.)	χ_m (calc.) Pascal
n-Hexyl methyl ketone	91·4	93·2	Acetoxime	44·4	42·3
*cyclo*Hexanone	62·0	60·6	Acetophenone oxime	79·9	81·4

For the oximes, agreement is poor in all but two cases. It is concluded that Pascal's method of calculation is not in general reliable for this class of compound. The more recent set of constants given by Pascal, Pacault, and Hoarau (*Compt. rend.*, 1952, **233**, 1078) is unlikely to give better agreement, particularly since it has a CH_2 increment of only 11·4, in spite of the fact that all recent experimental work, in various homologous series, indicates a value near to 11·7.

French and Harrison (*J.*, 1955, 1990) have shown that the observed susceptibilities of some simple organic compounds for which the Pascal system is unsatisfactory can

be better reproduced by a "Modified Bond Additivity System." In this, the molar susceptibility is expressed as the sum of terms characteristic of each bond in the molecule, together with a small number of bond-interaction terms. It was hoped that this system would serve as a better basis for the discussion of the present results. Unfortunately, it is not possible to determine independently all the bond or interaction terms required for the calculation of the susceptibilities of oximes and oxime ethers, owing to the scarcity of measurements on other organic compounds containing nitrogen. This difficulty can be overcome, for the present purpose, by treating the sum of a number of bond and interaction terms as a single term β. Then, by using the notation and numerical values of the previous paper (*J.*, 1955, 1990) the susceptibility of acetoxime can be written as:

$$\begin{aligned}\chi_m &= 6\chi_{C\text{-}H} + 2\chi_{C\text{-}C} + \chi_{O\text{-}H} + \chi_{C\text{-}N} + \chi_{N\text{-}O} + 2\lambda_{C\text{-}C\text{-}N} + \lambda_{O\text{-}N\text{=}C} - \lambda_{C\text{-}C\text{-}C}\\ &= 6\chi_{C\text{-}H} + 2\chi_{C\text{-}C} + \chi_{O\text{-}H} - \lambda_{C\text{-}C\text{-}C} + \beta\\ &= 35{\cdot}85 + \beta\end{aligned}$$

Similar calculations can be carried out for the other oximes and oxime ethers, provided the assumption is made that the interaction terms depend principally on the multiplicity and steric relationship of the bonds concerned, and only to a negligible extent on the particular atoms. This was shown to be reasonable in the previous work on compounds containing only carbon, hydrogen, and oxygen, and its use here enables relationships such as $\lambda_{N\text{-}O\text{-}C} = \lambda_{C\text{-}O\text{-}C}$ to be used.

It was found that when a "theoretical" susceptibility value had been calculated in this way for each compound studied, the value of β required to produce agreement with the experimental value varied considerably from compound to compound. The values suggested earlier for the bond terms such as $\chi_{C\text{-}C}$, although indicating the general principles of the method, may, as observed previously, require modification in the light of subsequent experimental work. In the more complex structures inaccuracies in assessing the contributions to the susceptibility from parts of the molecule other than the oxime group may be partly responsible for the observed variation in β. This possibility can be avoided by comparing, instead of the actual susceptibility values, the differences: χ_m(oxime or oxime ether) $-\chi_m$(carbonyl compound), which should be practically independent of errors in the fundamental constants. In Table 4 are given D, the experimental value of this difference, and the value of β required to produce agreement between experimental and calculated values of D. (*Note.* Throughout this section, all susceptibility values are recorded in 10^{-6} c.g.s. units and the negative signs are omitted.)

TABLE 4.

Substance	D	β	Substance	D	β
Acetoxime	10·6	8·65	*cyclo*Hexanone oxime	9·5	7·55
Ethyl methyl ketoxime	11·7	9·75	Acetoxime *O*-methyl ether	21·1	8·45
Diethyl ketoxime	10·2	8·25	Acetophenone oxime *O*-methyl ether	19·8	7·15
n-Hexyl methyl ketoxime	11·2	9·25	*cyclo*Hexanone oxime *O*-methyl ether	21·0	8·35
Acetophenone oxime	7·4	5·45	Acetoxime *O*-benzyl ether	71·1	7·61
*iso*Butyraldoxime	8·8	7·85			

There are two important facts which can be deduced from this Table. First, the value of the molar susceptibility increment associated with the transition

$$>C{=}O \longrightarrow >C{=}N{\cdot}OH \text{ (or } >C{=}O \longrightarrow >C{=}N{\cdot}O{\cdot}CH_3)$$

is not independent of the nature of the rest of the molecule. Secondly, in spite of the elimination of possible errors in contributions assigned to other parts of the molecule, a constant value of β is not obtained. Hence it appears that the simple modified scheme will not satisfactorily account for the susceptibilities of oximes and oxime ethers. If the very low value for acetophenone oxime (this compound is very difficult to purify adequately or to pack uniformly into a susceptibility tube) is neglected the values of β lie between 7·15 and 9·75. Whilst this variation is not large, it is greater than normally observed by the use of this system.

In order to explain the breakdown of the modified scheme in this case, a search was

made for previously recorded examples of a similar type. A case of considerable interest is the system of methyl-substituted ethylenes (Lacher, Pollock, Johnson, and Park, *J. Amer. Chem. Soc.*, 1951, **73**, 2838). These authors were only able to interpret the observed susceptibilities by the inclusion of interaction terms between *groups* both parallel and perpendicular to the double bond. We have verified that in this case also our scheme will not satisfactorily account for the experimental values, divergences being similar to those obtained with the oximes. It has already been shown that the system is satisfactory for certain compounds containing double bonds, *e.g.*, carbonyl compounds. Oximes and substituted ethylenes differ from carbonyl compounds in that substituent groups are attached to the atoms at both ends of the double bond.

The modified system implicitly includes interactions between groups attached to the same atom (in the form of bond interactions) but ignores interactions between groups attached to different ends of a double bond. Further, the interactions between *gem.*-dialkyl groups, as calculated by the system in its present form, would be independent of the particular alkyl groups concerned. The bond angles in acetoxime (Bierlin and Lingafelter, *Acta Cryst.*, 1951, **4**, 450) seem to indicate that the methyl and hydroxyl groups are sufficiently close for some kind of interaction to occur. It is suggested that neglect of the parallel type of interactions, and oversimplified treatment of the perpendicular type, are at least partly responsible for the breakdown of the system in this case. Any system of calculation satisfactory for unsaturated compounds must allow for these interactions, but the best method cannot be decided upon until more experimental values for simple unsaturated compounds become available.

With regard to the actual values of β given in Table 4, it may be significant that the symmetrical ketoximes ($R_2C{:}N{\cdot}OH$) give values of β very roughly 1 unit less than the corresponding unsymmetrical compounds ($RR'C{:}N{\cdot}OH$). A similar alternation effect is evident in the susceptibilities of the ketones themselves.

Finally, other factors bearing on the observed susceptibilities may be :

Tautomerism.—The lack of constancy of β values for the oxime ethers, in which tautomerism is impossible, prevents any definite conclusions being drawn about the influence of tautomerism in the oximes on the variation in β in the latter.

Geometrical Isomerism.—The variations in β values cannot be explained completely by varying amounts of *cis*- and *trans*-forms since the symmetrical oximes, which are incapable of geometrical isomerism, fail to yield a constant value of β. If *cis*- and *trans*-forms do have different susceptibilities, this may be due to the operation of the parallel type of interaction term previously discussed.

Difference in Susceptibility between Liquid and Solid States.—In spite of many investigations, it is still not completely certain how large a change in susceptibility (if any) accompanies the change of state from liquid to solid. There is no evidence of a systematic difference between the values of β found for solids and liquids in the present work, high and low values being found in both states.

Whilst not affecting the value of the method for systems of the type discussed in our previous paper, the present work does indicate that the modified bond-additivity system will not deal satisfactorily with all types of unsaturated compounds, unless further interaction terms are included, the investigation of which is proceeding.

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N-Hydroxy-imides. Part II. Derivatives of Homophthalic and Phthalic Acids.*

By D. E. Ames and T. F. Grey.

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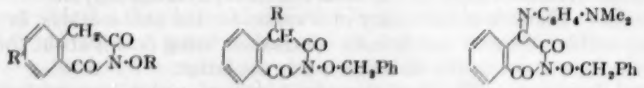
The *N*-benzyloxy- and *N*-hydroxy-imides of homophthalic, 4-chloro-homophthalic, 4-dimethylamino-homophthalic, phthalic, and naphthalic acids have been prepared. Further evidence on the structure of "phthaloxime" is presented.

It has been shown previously (Part I*) that the condensation of benzyloxyamine with dibasic acids yields *N*-benzyloxy-imides which can be catalytically hydrogenated to the *N*-hydroxy-imides or tautomeric products. This work has now been extended to the preparation of derivatives of some aromatic dibasic acids.

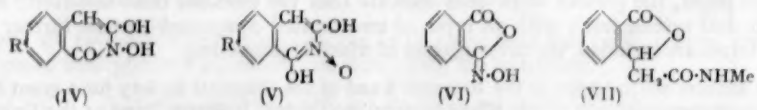
N-Benzyloxyhomophthalimide (I; R = CH_2Ph, R′ = H) was readily prepared in high yield by this method but, although various solvents were used, only small yields of the imides could be obtained from 4-chloro- and 4-dimethylamino-homophthalic acid. The corresponding *N*-hydroxyimides were prepared by catalytic hydrogenation. Two attempts were made to prepare derivatives of the imide (I) bearing a basic substituent in the α-position. First, treatment of (I; R = CH_2Ph, R′ = H) with benzenediazonium chloride gave the α-phenylazo-compound, reductively acetylated to the acetamido-imide (II; R = NHAc). The α-amino-imide could not, however, be obtained either by partial hydrolysis of this amide or by hydrogenation of the intermediate azo-compound. Condensation of the imide (I; R = CH_2Ph, R′ = H) with *NN*-dimethyl-*p*-nitrosoaniline yielded the derivative (III) (cf. Buu-Hoï, *Bull. Soc. chim. France*, 1945, **12**, 313) but this on



(I) (II) (III)

hydrogenation gave *p*-aminodimethylaniline. The infrared absorption spectra of these benzyloxy- and hydroxy-compounds exhibit the two characteristic imide bands (see Table); in the solid state, these products are therefore represented by the structures (I; R = H, R′ = H, Cl, or NMe_2) rather than as the tautomers (IV) and (V). This conclusion is of interest since the comparable *N*-hydroxy-αβ-dimethylglutaconimide exists as the enol (Part I).

On titration with alkali both *N*-benzyloxy- and *N*-hydroxy-homophthalimides show pK_a values of *ca.* 8, which must therefore correspond to ionisation of the enolised CH_2·CO group; the *N*-hydroxy-group is an extremely weak acid (pK_a 11·9).



(IV) (V) (VI) (VII)

N-Hydroxyphthalimide was prepared similarly and found to be identical with "phthaloxime," obtained from phthalic anhydride and hydroxylamine. Earlier work on the structure of this product has been examined by Brady, Baker, Goldstein, and Harris (*J.*, 1928, 529; cf. Hurd, Buess, and Bauer, *J. Org. Chem.*, 1954, **19**, 1140) who formulated it as phthalic anhydride mono-oxime (VI). We have been unable to prepare the yellow "isomer" described by Brady *et al.* and earlier workers. Putokhin (*J. Russ. Phys. Chem. Soc.*, 1930, **62**, 2203) apparently obtained the same product from *N*-ethoxycarbonylphthalimide and hydroxylamine and regarded it as *N*-hydroxyphthalimide. This structure

* The paper *J.*, 1955, 631, is regarded as Part I.

is indicated by the present method of preparation and is also supported by the following observations: (i) *N*-benzyloxy- and *N*-hydroxy-phthalimide show imide absorption bands similar to those of the *N*-ethyl-imide (see Table) though at somewhat higher frequencies (cf. Part I); (ii) the ultraviolet absorption spectra are also similar to those of phthalimide; and, (iii) the pK_a value (7·0) is well outside the normal range for oximes (Parke and Davis, *Analyt. Chem.*, **1954**, **26**, **642**, give pK_a *ca.* 10—12).

In the hope of preparing analogous seven-membered ring imides from *o*-carboxycinnamic acid, the condensation of the acid with methylamine was first studied. The only product isolated, however, was (VII), the infrared spectrum showing bands at **1567**, **1647**, and **3367** cm.$^{-1}$ (CO·NH) and at **1761** cm.$^{-1}$ (phthalide ring; cf. Grove and Willis, *J.*, **1951**, 882). Gabriel and Michael (*Ber.*, **1877**, **10**, 2203) obtained the parent phthalidylacetic acid by heating *o*-carboxycinnamic acid.

Absorption spectra and pK_a *values.*

	In ethanol		In soln., pH 8·9		Imide bands [a]	Other bands [a] 1640—2000	
	$\lambda_{max.}$	ε	$\lambda_{max.}$	ε	(cm.$^{-1}$)	(cm.$^{-1}$)	pK_a
(I; R = CH_2Ph, R′ = H)	2425	18,300	2450	15,400	1695	—	8·2 [b]
	2930	2100					
	3080	2200	2800 *	2200	1727		
(I; R = R′ = H)	2250 *	10,600	2975	3900	1667	—	8·0, 11·9 [b]
	2300	10,600			1727		
	2380 *	10,000					
(II; R = NHAc)	2450	22,100	2460	16,200	1709	1650	6·3 [b]
	3000 *	2100	2825	3900	1751		
(I; R = CH_2Ph, R′ = Cl)	2325 *	19,300	3100	17,900	1690	—	8·48 [c]
	3160	9800			1735 *		
(I; R = H, R′ = Cl)	3140	9000	2560	19,000	1701	1662	7·34 [d]
			3025	9100	1742		
(I; R = CH_2Ph, R′ = NMe_2)	2470	26,600	2350	27,600	1694	—	9·90 [e]
(I; R = H, R′ = NMe_2)	2360	14,200	2210	13,600	1717	—	8·97 [f]
	2470 *	13,600	2630	10,900	1658		
			3300	3500			
Phthalimide	2150	41,000	—	—	—	—	—
	2295	16,200					
	2380	10,700					
	2910	1400					
N-Ethylphthalimide	—	—	—	—	1724	—	—
					1779		
N-Benzyloxyphthalimide ...	2220	47,200	—	—	1733	—	—
	2960	2100			1792		
N-Hydroxyphthalimide ...	2205	30,300	—	—	1745	1721	7·0 [g]
	2980	1600			1795	1866	
N-Acetoxyphthalimide ...	2180	43,000	—	—	1751	1821 [h]	—
	2375	9500			1792	1862	
	2950	1900					
N-Benzyloxynaphthalimide	2135	26,600	—	—	1692	—	—
	2340	37,900			1709		
	2355	12,800					
	4550	360					
N-Hydroxynaphthalimide	2360	38,400	—	—	1666	—	8·25 [g]
	3350	11,900			1715		

* Inflection. [a] Nujol mulls. [b] 50% Dimethylacetamide. [c] 75% Ethanol. [d] 50% Ethanol. [e] 75% Dimethylformamide. [f] 50% Dimethylformamide. [g] 50% Methanol. [h] Acetate band.

Experimental

N-Hydroxyphthalimide.—Phthalic anhydride (2·0 g.) and benzyloxyamine (1·7 g.) were refluxed with xylene (50 c.c.) until no more water could be separated. Evaporation *in vacuo* and crystallisation from ethanol furnished needles of *N-benzyloxyphthalimide* (3·1 g.; 90%) (Found: C, 71·7; H, 4·4; N, 5·3. $C_{15}H_{11}O_3N$ requires C, 71·1; H, 4·4; N, 5·5%). Hydrogenation of this imide (20 g.) in ethyl methyl ketone (100 c.c.) over palladised strontium carbonate (3 g.; 5% Pd) yielded the *N*-hydroxy-imide (9·5 g.; 74%), rods, m. p. 232—233° (decomp.), from ethyl methyl ketone (Found: C, 58·8; H, 3·1; N, 8·4. Calc. for $C_8H_5O_3N$: C, 58·9; H, 3·1; N, 8·6%). The melting point was not depressed on admixture with material prepared as described

by Orndorff and Pratt (*Amer. Chem. J.*, 1912, **47**, 99); the infrared spectra of the samples were also identical. The acetate had m. p. 185—186° (Orndorff and Pratt give m. p. 183—185°).

N-Hydroxynaphthalimide.—Prepared in the same manner, *N-benzyloxynaphthalimide* (55%) separated from ethyl methyl ketone–light petroleum (b. p. 60—80°) in needles, m. p. 187—188° (Found: C, 75·0; H, 4·4; N, 4·9. $C_{19}H_{13}O_3N$ requires C, 75·2; H, 4·3; N, 4·6%). Catalytic debenzylation gave the hydroxy-imide which had m. p. 280—281° (from ethanol), undepressed on admixture with product prepared by Jaubert's method (*Ber.*, 1895, **28**, 362) (Found: C, 67·2; H, 3·3; N, 6·6. Calc. for $C_{12}H_7O_3N$: C, 67·6; H, 3·3; N, 6·6%).

N-Hydroxyhomophthalimide.—*N-Benzyloxyhomophthalimide* (83%), prepared by the same procedure, formed prismatic needles (from ethanol), m. p. 143—144° (Found: C, 71·8; H, 4·8; N, 5·4. $C_{16}H_{13}O_3N$ requires C, 71·9; H, 4·9; N, 5·2%). Hydrogenation afforded the *hydroxy-imide*, rods, m. p. 199—200°, from ethyl methyl ketone (Found: C, 61·4; H, 4·1; N, 7·8. $C_9H_7O_3N$ requires C, 61·0; H, 4·0; N, 7·9%).

4-Dimethylaminohomophthalic Acid.—4-Nitrohomophthalic acid (20·0 g.) (Ungnade, Nightingale, and French, *J. Org. Chem.*, 1945, **10**, 535) in methanol (100 c.c.) was hydrogenated in the presence of palladised strontium carbonate (2·0 g.; 5% Pd). When 3 mol. of hydrogen had been absorbed, formaldehyde (40 c.c.; 36%) was added and hydrogenation was continued. After addition of water (150 c.c.), the boiling solution was filtered; on cooling the *amino-acid* (13·2 g.) separated and formed thick parallelograms, m. p. 215—216° (decomp.), from methanol (Found: C, 59·2; H, 5·9; N, 6·3. $C_{11}H_{13}O_4N$ requires C, 59·2; H, 5·9; N, 6·3%).

4-Chlorohomophthalic Acid.—The nitro-acid (32 g.) in methanol (200 c.c.) was hydrogenated as before, water added, and the boiling solution filtered. Evaporation under reduced pressure gave the crude 4-aminohomophthalic acid which was dissolved in hydrochloric acid (250 c.c.; 2N) and diazotised by the addition of sodium nitrite (9·4 g.) in water (30 c.c.). The solution was added to cold cuprous chloride (from 160 g. of hydrated cupric sulphate) in concentrated hydrochloric acid. After 2 hr. the *chloro-acid* (16·0 g.) was filtered off and recrystallised from water forming needles, m. p. 191—192° (Found: C, 50·0; H, 3·3; Cl, 16·0. $C_9H_7O_4Cl$ requires C, 50·4; H, 3·3; Cl, 16·5%).

Substituted Homophthalimides.—Owing to insolubility, the condensation of 4-chloro- and 4-dimethylamino-homophthalic acids with benzyloxyamine failed except in boiling *o*-dichlorobenzene. The acid was dissolved in hot solvent and, after addition of the benzyloxyamine, the mixture was distilled slowly until no more water was eliminated (*ca.* 1/2 hr.). Evaporation under reduced pressure furnished the crude product which was recrystallised.

N-Benzyloxy-4-chlorohomophthalimide (40%) formed needles, m. p. 163—164°, from ethanol–ethyl methyl ketone (Found: C, 63·7; H, 4·0; N, 4·8; Cl, 12·1. $C_{16}H_{12}O_3NCl$ requires C, 63·8; H, 4·0; N, 4·7; Cl, 11·8%).

N-Benzyloxy-4-dimethylaminohomophthalimide (35%) separated from ethanol in plates, m. p. 158—160° (Found: C, 69·9; H, 6·0; N, 9·1. $C_{18}H_{18}O_3N_2$ requires C, 69·7; H, 5·9; N, 9·0%).

The following were obtained by catalytic hydrogenation: *4-Chloro-N-hydroxyhomophthalimide* (70%), needles, m. p. 215—216°, from ethyl methyl ketone (Found: C, 51·5; H, 3·1; N, 6·7; Cl, 16·9. $C_9H_6O_3NCl$ requires C, 51·5; H, 2·9; N, 6·6; Cl, 16·8%). *4-Dimethylamino-N-hydroxyhomophthalimide*, yellow cubes, m. p. 158—159°, from ethanol (Found: C, 55·2; H, 6·0; N, 11·5. $C_{11}H_{12}O_3N_2,H_2O$ requires C, 55·5; H, 5·9; N, 11·8%). This compound could be sublimed unchanged at 130—150°/0·05 mm. (Found: C, 55·2; H, 6·0; N, 11·9%) but the spectra and especially pK_a values indicate that it is a hydrate and not a hydrolysis product.

N-Benzyloxy-α-phenylazohomophthalimide.—To *N*-benzyloxyhomophthalimide (2·0 g.) in sodium hydroxide solution (35 c.c.; 2N), acetic acid (3·5 c.c.) and benzenediazonium chloride solution (from aniline, 1·6 g.) were added, successively. The precipitate was crystallised from ethyl methyl ketone, giving red prisms of the *azo-compound* (0·9 g.), m. p. 214—215° (Found: C, 70·9; H, 4·7; N, 11·4. $C_{22}H_{17}O_3N_3$ requires C, 71·2; H, 4·6; N, 11·3%).

α-Acetamido-N-benzyloxyhomophthalimide.—The azo-compound (10 g.) was added in portions to a stirred mixture of zinc (10 g.), acetic acid (20 c.c.), and acetic anhydride (9 c.c.). Small portions of zinc and acetic anhydride were added at intervals until the yellow colour disappeared (8 hr.). The collected solid was washed with acetic acid (100 c.c.), and the combined filtrates evaporated under reduced pressure. Trituration of the residual gum with ether yielded the crude product (6·0 g.; m. p. 150—156°). The *acetamido-imide* crystallised from ethyl methyl ketone in needles, m. p. 172—173° (Found: C, 66·9; H, 4·6; N, 8·6; Ac, 13·1. $C_{18}H_{16}O_4N_2$ requires C, 66·7; H, 5·0; N, 8·6; Ac, 13·3%).

N-Benzyloxy-α-p-dimethylaminophenylimino)homophthalimide (cf. Buu-Hoï, *Bull. Soc. chim. France*, 1945, **12**, 313).—*NN*-Dimethyl-*p*-nitrosoaniline (4·4 g.) in hot ethanol (60 c.c.) was

added to a hot solution of *N*-benzyloxyhomophthalimide (7·9 g.) in ethanol (175 c.c.), and the mixture refluxed for 30 min. When the solution cooled the *imide* (8·6 g.) crystallised in violet, prismatic needles, m. p. 138—140° (Found: C, 71·8; H, 5·4; N, 10·4. $C_{24}H_{21}O_3N_3$ requires C, 72·2; H, 5·3; N, 10·5%).

Reaction of o-Carboxycinnamic Acid with Methylamine.—The acid (2 g.) and ethanolic methylamine (10 c.c.; 33%) were heated at 180° (bath) for 10 min., the solvent being allowed to distil off, and then at 225° for 10 min. Crystallisation of the residue from ether–methanol gave a product (0·4 g.), m. p. 138—142°. The pure *N-methylphthalidylacetamide* formed needles, m. p. 144—145°, from methanol (Found: C, 64·3; H, 5·4; N, 6·6. $C_{11}H_{11}O_3N$ requires C, 64·4; H, 5·4; N, 6·8%).

The authors are grateful to Dr. R. E. Bowman for helpful suggestions and advice; they are also indebted to Miss E. M. Tanner, Dr. J. M. Vandenbelt, and Mr. R. B. Scott for the potentiometric titrations and spectroscopic data, and to Mr. A. J. Durre for some of the microanalyses.

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Conjugated Macrocycles. Part XXVI. Octamethyltetrazaporphin.*

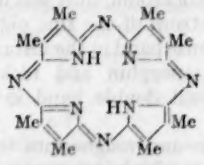
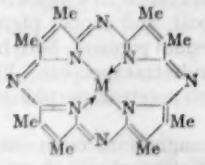
By M. E. BAGULEY, H. FRANCE, R. P. LINSTEAD, and MARGARET WHALLEY.

[Reprint Order No. 6281.]

The reaction of dimethylmalei- and dimethylfumaro-nitriles with various organomagnesium compounds gave magnesium octamethyltetrazaporphin (II; M = Mg). Removal of magnesium from this compound yielded the metal-free pigment (I) which was converted into the copper, nickel, cobalt, and zinc pigments (II; M = Cu, Ni, Co, or Zn). Their structures have been established by analogy with other tetrazaporphins and by degradation.

THE synthetical methods described for the preparation of tetrazaporphin from maleinitrile (Linstead and Whalley, *J.*, 1952, 4839) are now applied to the preparation of octaalkyltetrazaporphins (France, Jones, and Imperial Chemical Industries Limited, B.P. 689,387, 689,388, 689,389; France and Imperial Chemical Industries Limited, B.P. 721,763; Linstead, Whalley, and Ficken, B.P. 713,208). Of these the simplest is octamethyltetrazaporphin (I) in which there are no complications of positional isomerism.

Octamethyltetrazaporphins were readily prepared from dimethylmalei- and dimethylfumaro-nitrile (Piggott and Beech, *J.*, 1955, 423) by the use of solutions obtained by decomposing methylmagnesium iodide with alcohols (Ficken and Linstead, *J.*, 1952, 4846). Of the large number of alcohols examined, *n*-butanol and *n*-pentanol were the most satisfactory. The action of dimethylfumaronitrile on a decomposed Grignard reagent in butanol or *iso*pentanol gave magnesium octamethyltetrazaporphin (II; M =

(I)  (II) 

Mg) in *ca.* 50% yield. *n*-Butanol was used for preference as slightly higher and more consistent yields were obtained. Dimethylfumaronitrile is to be preferred to the *cis*-isomeride for preparative purposes on account of its greater availability.

Magnesium octamethyltetrazaporphin, like the magnesium derivatives of other macrocycles, forms various solvates. Of these only the monopentanolate was obtained analytically pure. The alcohol was removed from this by heating it at 10^{-5} mm., to give the unsolvated

* Part XXV, *J.*, 1954, 2490.

magnesium octamethyltetrazaporphin. Treatment with absolute ethanol then gave a crystalline product which contained between one and two mols. of ethanol.

The metal was easily removed from magnesium octamethyltetrazaporphin with boiling glacial acetic acid, to yield crystalline octamethyltetrazaporphin (I). Demetallation with mineral acids caused partial or complete breakdown of the macrocycle (cf. Linstead and Whalley, *loc. cit.*; Ficken and Linstead, *loc. cit.*).

Octamethyltetrazaporphin forms a series of metal derivatives. These show two characteristics noted before for metallic phthalocyanines and other similar macrocyclic pigments : first, there is a tendency for the metal derivatives to form mixed crystals with the parent compound; secondly, several of the derivatives form solvates, and the tendency to do this depends upon the metal.

Copper octamethyltetrazaporphin (II; M = Cu) was obtained by reaction of the metal-free pigment with copper bronze in boiling *o*-dichlorobenzene. In chlorobenzene the reaction did not proceed to completion and mixed crystals of metal-free and copper pigments were obtained. Nickel and zinc octamethyltetrazaporphins (II; M = Ni and M = Zn) were obtained by extracting the metal-free pigment into boiling *o*-dichlorobenzene containing a large excess of anhydrous nickel chloride or zinc acetate. Direct refluxing of metal-free pigment with the metallic salt invariably gave a mixture. The zinc compound (the only known zinc tetrazaporphin other than zinc phthalocyanine) was obtained in an unsolvated form by crystallisation from chlorobenzene but from pyridine gave a solvate containing about 1 mol. of pyridine. The pigment thus shows some resemblance to zinc phthalocyanine which has now been found to give a monopyridine solvate, which is stable at 120°/10 mm.

The physical properties of the octamethyltetrazaporphins are closely similar to those of the tetra*cyclo*hexenotetrazaporphins (Ficken and Linstead, *loc. cit.*). They are more stable to heat and to mineral acids than the unsubstituted tetrazaporphins but are not sufficiently stable to heat to permit the use of sublimation for purification or for the growth of large crystals.

The solubilities in organic solvents are low. The metal-free compound is very sparingly soluble in chlorobenzene, to give a violet-blue non-fluorescent solution (cf. tetrazaporphin). The zinc and magnesium pigments are slightly soluble in hot chlorobenzene (non-fluorescent solutions) but completely insoluble in the cold. The magnesium pigment is fairly soluble in the higher primary alcohols : both the magnesium and the zinc pigment dissolve in cold pyridine, giving blue solutions with a strong fluorescence, crimson in daylight and brilliant vermilion (indistinguishable from that of magnesium tetra*cyclo*hexenotetrazaporphin) in ultraviolet light. Magnesium octamethyltetrazaporphin, like other magnesium macrocycles (including chlorophyll), gives a bright red chemiluminescence when added to hot hydrocarbon solvents, such as tetralin, containing peroxide.

The light absorptions of all the pigments have been measured over the range 3000—10,000 Å and correspond closely to those of the tetra*cyclo*hexenotetrazaporphins, a hypsochromic shift of about 20 Å being observed for the main peaks in the visible region for the magnesium and metal-free pigments. A small bathochromic shift was noted in the case of the nickel, cobalt, and copper pigments. The spectrum of the zinc pigment resembles that of the magnesium pigment, both having a very intense band in the ultraviolet spectrum. Nickel octamethyltetrazaporphin, like nickel tetrazaporphin and nickel and palladium tetra*cyclo*hexenotetrazaporphin, shows an unusual double band in the ultraviolet spectrum.

Solutions of magnesium octamethyltetrazaporphin and magnesium tetra*cyclo*hexeno-tetrazaporphin (unlike those of magnesium tetrazaporphin) decomposed quite rapidly in daylight. A solution of each was left out of doors from June to September and the almost decolorised solutions were examined. The magnesium octamethyltetrazaporphin solution gave an almost 50% yield of dimethylmaleimide and a small amount of unidentified oil. Magnesium tetra*cyclo*hexenotetrazaporphin under similar conditions gave 3 : 4 : 5 : 6-tetrahydrophthalimide.

The close similarity at every point between octamethyl- and tetra*cyclo*hexeno-tetrazaporphins leaves little doubt as to the structures of the former compounds, and this was

conclusively confirmed as follows: Oxidation of metal-free octamethyltetrazaporphin with chromium trioxide in sulphuric acid (cf. Fischer and Walach, *Annalen*, 1926, **450**, 180; Muir and Neuburger, *Biochem. J.*, 1949, **45**, 163; Ficken and Linstead, *loc. cit.*) gave an 80% yield of dimethylmaleimide, thus showing that formation of the pigment had not created new C–C bonds. The nitrogen content of the aqueous layer after extraction of the imide, corresponded to four aza-links. Oxidation with ceric sulphate by the method used for the phthalocyanines (Dent, Linstead, and Lowe, *J.*, 1934, 1036) gave results higher than the 1 atom of oxygen required for the degradation of one molecule of pigment. This was probably due to subsequent oxidation of the double bond of the imide.

Alternative methods for the preparation of tetrazaporphins from dimethyl-malei- and -fumaro-nitrile were tried. Nickel, cobalt, and traces of copper octamethyltetrazaporphin were obtained by the urea-melt method (cf. Linstead and Whalley, *loc. cit.*). Because of the very high volatility of dimethylfumaronitrile, urea-melt reactions with this nitrile were carried out in sealed tubes. Sodium and lithium alkoxides, successful for the preparation of phthalocyanines and tetra*cyclo*hexenotetrazaporphins, gave very low yields of octamethyltetrazaporphins because of decomposition of the nitrile in alkaline solution. Magnesium alkoxides (cf. magnesium tetrazaporphin) reacted very slowly with dimethylfumaronitrile to give lower yields of magnesium octamethyltetrazaporphin than those obtained by the Grignard-reagent method.

Dimethylmalei- and dimethylfumaro-nitrile both give tetrazaporphin pigments much more readily, and in better yield than the unsubstituted maleinitrile (Linstead and Whalley, *loc. cit.*). However, they showed less tendency to pigment formation than phthalonitrile and, as was to be expected, reacted in much the same way as **3 : 4 : 5 : 6**-tetrahydrophthalonitrile (Ficken and Linstead, *loc. cit.*).

The ease of formation of pigments from dimethylfumaronitrile is somewhat surprising as intermediates with a *cis*-configuration must be involved in forming the pyrrole-like corners of the azaporphin ring. Fumaronitrile itself shows no detectable tendency to pigment formation. Clearly an inversion of configuration occurs in the dimethyl series at some stage in there action sequence. Dimethylmaleinitrile is completely isomerised by ammonium toluene-*p*-sulphonate at 200°.

Experimental

Continuous extractions of macrocyclic pigments were carried out with an all-glass modification of the "hot extraction" apparatus described by Barrett, Dent, and Linstead (*J.*, 1936, 1726).

Magnesium Octamethyltetrazaporphin.—Dry *n*-butanol (75 c.c.) was slowly added to cooled, ethereal methylmagnesium iodide (prepared from 3 g. of magnesium), and the ether was allowed to evaporate. Dimethylfumaronitrile (12 g.) was then added and the mixture refluxed for 6 hr. The *n*-butanol was evaporated under reduced pressure and the residue triturated with water and washed with aqueous ethanol (1 : 1) until the washings were colourless. Extraction of the residue with dry *n*-pentyl alcohol gave dark blue needles, with a bronze reflex, of *magnesium octamethyltetrazaporphin monopentanolate* (8·4 g., 55%) (Found: C, 64·7; H, 7·2; N, 20·4. $C_{29}H_{36}N_8OMg$ requires C, 64·9; H, 6·7; N, 20·9%). Heating the solvate at 185°/10^{-5} mm. gave *magnesium octamethyltetrazaporphin* (Found: C, 64·6; H, 5·7; N, 24·5; Mg, 5·6. $C_{24}H_{24}N_8Mg$ requires C, 64·3; H, 5·4; N, 25·0; Mg, 5·4%). Treatment of the unsolvated material with absolute ethanol gave an *ethanolate* (Found: C, 62·8; H, 6·4; N, 22·7. $C_{24}H_{24}N_8Mg,2C_2H_5{\cdot}OH$ requires C, 63·2; H, 6·1; N, 22·7%).

Metal-free Octamethyltetrazaporphin.—Magnesium octamethyltetrazaporphin monopentanolate (8·4 g.) was boiled with glacial acetic acid (50 c.c.) for 15 min. Water (200 c.c.) was added and the solid filtered off and washed with water and ethanol. The residue was extracted with chlorobenzene, *octamethyltetrazaporphin* crystallising as purple prisms (4·5 g., 65%) from the extract (Found: C, 67·4; H, 6·3; N, 26·0. $C_{24}H_{26}N_8$ requires C, 67·6; H, 6·1; N, 26·3%).

Other Metal Derivatives.—The metal-free pigment (1·0 g.) was extracted into boiling *o*-dichlorobenzene (60 c.c.) containing anhydrous nickel chloride (10 g.). When extraction was complete, the mixture was boiled for 1 hr. and allowed to cool. The solid was filtered off and washed with light petroleum. The excess of nickel chloride was washed out with water and the dried residue extracted with chlorobenzene. *Nickel octamethyltetrazaporphin* (0·89 g., 78%) crystallised

as purple prisms with a bronze reflex from the extract (Found: C, 59·7; H, 5·1; N, 23·0; Ni, 11·7. $C_{36}H_{24}N_8Ni$ requires C, 59·7; H, 5·0; N, 23·2; Ni, 12·2%).

The *zinc* pigment (0·91 g., 79%) was prepared similarly from the metal-free pigment (1·0 g.) and zinc acetate (10 g.) and crystallised from chlorobenzene (Found: C, 59·0; H, 5·1; N, 23·0; Zn, 13·7. $C_{36}H_{24}N_8Zn$ requires C, 58·9; H, 4·9; N, 22·9; Zn, 13·4%). Crystallisation from pyridine gave an indefinite *pyridine solvate* (Found: C, 60·6; H, 5·7; N, 20·9. $C_{29}H_{29}N_9Zn$ requires C, 61·2; H, 5·1; N, 22·2%).

The metal-free pigment (100 mg.) was refluxed with copper bronze (1 g.) in *o*-dichlorobenzene (50 c.c.) for 3 hr. The mixture was then cooled and filtered and the solid extracted with chlorobenzene, giving *copper octamethyltetrazaporphin* (49 mg., 42%) (Found: C, 59·3; H, 5·2; N, 23·5; Cu, 12·7. $C_{24}H_{24}N_8Cu$ requires C, 59·0; H, 4·9; N, 23·0; Cu, 13·0%).

Urea-melt Method.—(i) *Nichel octamethyltetrazaporphin.* A mixture of dimethylmaleinitrile (1·06 g.), urea (5·0 g.), anhydrous nickel chloride (0·5 g.), ammonium molybdate (0·1 g.), and nitrobenzene (6 c.c.) was stirred at 155—160° for 4 hr. The mixture was treated with 0·5N-hydrochloric acid (100 c.c.), and the nitrobenzene removed by steam-distillation. The filtered residue was stirred with 0·5N-sodium hydroxide at 60° for 15 min. The solid was filtered off, dried, and extracted with *o*-dichlorobenzene, to give nickel octamethyltetrazaporphin (0·13 g., 12%). (ii) The *cobalt* pigment (0·10 g., 9%) was prepared similarly, anhydrous cobaltous chloride (0·5 g.) being used (Found: C, 60·0; H, 5·7; N, 24·0; Co, 12·6. $C_{24}H_{24}N_8Co$ requires C, 59·6; H, 5·0; N, 23·2; Co, 12·2%).

Zinc Phthalocyanine Solvate.—Zinc phthalocyanine was recrystallised from pyridine, giving purple prisms of *zinc phthalocyanine pyridine solvate* (Found: C, 67·7; H, 3·5; N, 19·3. $C_{37}H_{21}N_9Zn$ requires C, 67·6; H, 3·2; N, 19·2%) which was stable at 120°/10 mm. Spectrum in pyridine: max. at 3475 (log ε 4·81), 6070 (4·59), 6460 (4·56), 6720 (5·45).

Oxidation of Octamethyltetrazaporphin.—A solution of the metal-free pigment (82 mg.) in concentrated sulphuric acid (2 c.c.) was cooled in ice-salt and poured on ice (3 g.). Chromium trioxide (85 mg.), dissolved in the minimum amount of water, was added and the mixture allowed to warm to room temperature until the pigment was completely oxidised. Excess of chromium trioxide was removed by treating the solution with ferrous sulphate (3 g.) in water (25 c.c.). The solution was extracted with ether overnight, and the ether-extracts were evaporated. Sublimation of the residue yielded dimethylmaleimide (75 mg., 80%), m. p. and mixed m. p. 119—120°.

The ammonium salts contained in the residual aqueous layer were determined by the Kjeldahl method (Found: N, 12·7. Calc. for 4 aza-links: N, 13·1%).

Photochemical Decomposition of Pigments.—(a) *Magnesium octamethyltetrazaporphin.* The pigment (200 mg.) was dissolved in pyridine (100 c.c.), and the solution exposed to daylight during June—August. Most of the fluorescence had then disappeared. The solution was filtered to remove precipitated magnesium salts, and the pyridine evaporated under reduced pressure. The residue was extracted with methanol, traces of pigment were removed by stirring the solution with charcoal, and the solvent was evaporated. Sublimation of the residue gave dimethylmaleimide (87 mg., 47%), m. p. and mixed m. p. 116—119°.

(b) *Magnesium tetra*cyclo*hexenotetrazaporphin* (with G. E. Ficken). A solution of magnesium tetra*cyclo*hexenotetrazaporphin pyridine hydrate (560 mg.) in pyridine (50 c.c.) was completely decolorised after treatment in the manner described above. The solution was filtered and evaporated to dryness under reduced pressure. Extraction with light petroleum (b. p. 60—80°) gave a trace of 3 : 4 : 5 : 6-tetrahydrophthalimide, m. p. 162—165°, mixed m. p. 164—167°. Extraction of the residue with benzene gave impure 3 : 4 : 5 : 6-tetrahydrophthalimide (79 mg., 15%).

Spectra.—During preparative work, absorption spectra (see Table) in the visible region were measured on a Hilger–Nutting spectrometer. For the measurement of intensities, a Unicam Spectrophotometer SP 500 was used, a hydrogen lamp being employed for readings below 4000 Å and a tungsten lamp for higher wavelengths. Solutions were prepared by boiling an

Pigment	Solvent	Absorption maxima (Å)				log ε			
Metal-free ...	PhCl	3430	5560	5970	6270	4·89	4·66	3·94	4·86
Magnesium ...	C_5H_{11}·OH	3420	5465	5950		4·96	4·23	5·08	
	C_5H_5N	3460	5480	5970		4·94	4·21	5·06	
Nickel	$C_6H_4Cl_2$	3210	3410	5470	5920	4·57	4·52	4·26	4·82
Copper	$C_6H_4Cl_2$	3430	5420	5930		4·83	4·19	5·02	
Zinc	C_5H_5N	3465	5510	5950		4·93	4·17	5·02	
Cobalt	C_6H_5Cl	3455	5420	5890		4·66	4·27	4·86	

accurately weighed amount (0·5—0·7 mg.) of the pigment with the solvent, cooling, and dilution to 100 c.c.

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Heterocyclic Imines and Amines. Part IV. Imidines from 3 : 4 : 5 : 6-Tetrahydrophthalic Acid and cis-Hexahydrophthalic Acid. An Unusual Dehydrogenation.*

By G. E. Ficken and R. P. Linstead.

[Reprint Order No. 6282.]

The preparation of 3 : 4 : 5 : 6-tetrahydrophthalimidine and of *cis*-hexahydrophthalimidine from the corresponding nitriles is described. The structures are established by hydrolysis. The imidines react with two mols. of primary bases with evolution of ammonia. The products have the expected structures except that the same diphenylimino-compound is obtained from both imidines, a novel type of dehydrogenation occurring with the hexahydro-compound. The properties, including light-absorption data, of the imidines and their derivatives are described and a preliminary account is given of their easy conversion into tetrazaporphin pigments.

It has been shown in earlier papers of this series (Elvidge and Linstead, *J.*, 1952, 5000; 1954, 442) that phthalonitrile and succinonitrile can, under suitable conditions, add the elements of ammonia to yield heterocyclic compounds, the imidines. This new class of compound has an interesting and specific chemistry of its own. In particular, the imidines are valuable precursors of tetrazaporphin pigments. We now report the preparation of the first imidine of the maleic acid series, 3 : 4 : 5 : 6-tetrahydrophthalimidine; also the related hexahydrophthalimidine. There is a considerable difference between the saturated and the unsaturated compound and we shall deal with the latter first, as the less complicated.

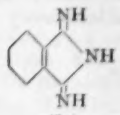
3 : 4 : 5 : 6-Tetrahydrophthalonitrile (Linstead and his co-workers, *J.*, 1952, 4846; 1954, 3730) readily adds ammonia in a boiling methanol solution containing a trace of sodium methoxide.† The product is a strong base, $C_8H_{11}N_3$, comparatively stable, and easily crystallised from ethanol or dimethylformamide. It is sparingly soluble in cold water and not apparently hydrolysed. It yields a monopicrate and a dihydrochloride. It does not melt but decomposes fairly sharply at 177—180° with the formation of (*inter al.*) tetra*cyclo*hexenotetrazaporphin. It is clearly the imidine (I) of tetrahydrophthalic acid from its method of preparation and because it is readily hydrolysed by boiling water first to the imino-imide (II; R = H) and more slowly to tetrahydrophthalimide (III). This formulation is also supported by the reactions with primary bases reported below. Two tautomeric structures can be written for the imidine, the di-imine (I*a*) and the imino-amine (I*b*). The diaminopyrrole type, a third possibility for the imidines of saturated acids, cannot apply here. We do not regard the available evidence on the fine structure as being conclusive and it is receiving further study. For the present the di-imine structure (I*a*) sufficiently accounts for the properties of the compound.

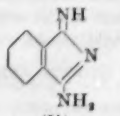
The imino-imide (II; R = H; Δ^8-hexahydro-1-imino-3-oxo*iso*indole) is also obtained by thermal isomerisation of 2-cyano-3 : 4 : 5 : 6-tetrahydrobenzamide (Ficken and Linstead, *J.*, 1952, 4846). It yields a monopicrate and a monohydrochloride. Like the related

* Part III, *J.*, 1954, 442.

† This modification of earlier methods is due to Imperial Chemical Industries Limited, Dyestuffs Division.

imino-imides investigated by Elvidge and Linstead (*loc. cit.*) it reacts with primary bases with elimination of ammonia. A phenylimino-compound (II; R = Ph) and an oximino-compound (II; R = OH) were formed in this way.


(I*a*)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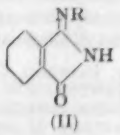
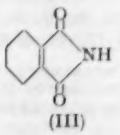
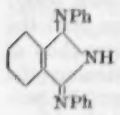

(II)

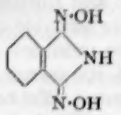

(III)

3 : 4 : 5 : 6-Tetrahydrophthalimidine also reacted readily with an excess of aniline or hydroxylamine, the products being the double condensation products (IV and V).

Hexahydrophthalimidine was less readily prepared than the tetrahydro-analogue. The method described above gave little or no product when applied to *cis*-hexahydrophthalonitrile and, although reaction with methanolic ammonia at higher temperatures gave some imidine, the yield was variable and never over 10%. The main trouble is the great reactivity of the hexahydroimidine which, even at 90°, tends to eliminate ammonia with the formation of aza-linked macrocyclic pigment and polymeric material. Below this temperature, reaction of the nitrile with ammonia is slow. Another difficulty is the great ease of hydrolysis of the imidine; on several occasions only the corresponding imino-imide was isolated. However, an alternative process, described by Elvidge and Linstead (*loc. cit.*, 1953) for the preparation of succinimidine, was successful, and when *cis*-hexahydrophthalonitrile was treated with a solution of sodamide in formamide the required imidine (octahydro-1 : 3-di-imino*iso*indole) (VI, or an isomer) crystallised from the reaction mixture in up to 70% yield.

Hexahydrophthalimidine is unstable and highly reactive. Prepared as described above, it forms colourless needles but it soon acquires a blue tinge, particularly when dried under


(IV)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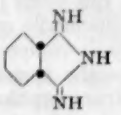
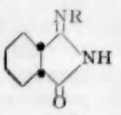
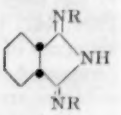

(VI)


(VII)


(VIII)

reduced pressure. The crystalline reaction product analysed for a hemihydrate, the water being lost at 10^{-5} mm. The base has no definite melting point. It forms a beautifully crystalline anhydrous monopicrate and a dihydrochloride. The imidine is hydrolysed when exposed to moist air and must be kept in a desiccator or a sealed vessel (unlike the tetrahydrophthalimidine, which seems to be indefinitely stable on the bench). Hexahydrophthalimidine dissolves readily in cold water with rapid hydrolysis to octahydro-1-imino-3-oxo*iso*indole (VII; R = H). The product is identical with the imino-imide described by Ficken, France, and Linstead, *J.*, 1954, 3730 and is hydrolysed by boiling water to *cis*-hexahydro-phthalimide. The imidine therefore has the *cis*-configuration.

trans-Hexahydrophthalonitrile reacts rather slowly with sodamide in formamide to yield an imidine indistinguishable from that described above. It gave the same picrate and was hydrolysed to the *cis*-imino-imide.

cis-Hexahydrophthalimidine reacts readily with hydroxylamine to give the dioximino-compound (VIII; R = OH). Reaction with aniline in boiling ethanol also leads to evolution of ammonia. The product, however, *is not the expected diphenylimine* (VIII; R = Ph) *but its dehydrogenation product*, that is the diphenylimine (IV) already obtained from 3 : 4 : 5 : 6-tetrahydrophthalimidine. This remarkable dehydrogenation has been repeated several times and we have no doubt as to its authenticity. A correspondingly easy passage from hexahydro- to tetrahydro-phthalic derivatives has not been observed with the parent imidine or the dioxime. The change, embodying, as it does, the introduction of a double bond into a substituted succinic acid system, is of considerable general interest. It is being investigated further. The fate of the extruded hydrogen is unknown; aerial oxygen is a possible acceptor.

The ultraviolet absorption data for these new compounds are summarised in the Table.

It will be seen that the light absorption of the hexahydro-compounds closely resembles that of the corresponding succinic derivatives (Elvidge and Linstead, *loc. cit.*, 1953). The question of fine structure is reserved for a later communication.

As has already been said, both these imidines, particularly *cis*-hexahydrophthalimidine, are intermediates in the formation of tetrazaporphins. A little tetra*cyclo*hexenotetrazaporphin (Ficken and Linstead, *loc. cit.*, 1952) is formed when the tetrahydrophthalimidine is prepared from the corresponding nitrile. When an alcoholic solution of the hexahydro-imidine is boiled, a magenta colour develops. This is stable when the solution is cooled in an inert atmosphere but becomes pale green in air. Prolonged boiling of a solution, especially in a higher-boiling alcohol, gives first an irreversible purple colour and subsequently deposition of solid pigment. The product is a mixture of tetra*cyclo*hexenotetrazaporphin (main bands at 628 and 560 mμ) and a blue hydrogenated pigment (bands

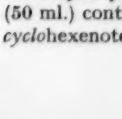
	3 : 4 : 5 : 6-*Tetrahydrophthalic series.*			*cis*-*Hexahydrophthalic series.*		
Compound	Formula	$\lambda_{max.}$ (mμ)	$10^{-3}\varepsilon$	Formula	$\lambda_{max.}$ (mμ)	$10^{-3}\varepsilon$
Imino-imide	II; R = H	240	10·5	VII; R = H	227	16·4
Oxime from imino-imide	II; R = OH	270 *	13·1	VII; R = OH	220 }	9·6
		281	13·8		227 }	
Phenylimine from imino-imide	II; R = Ph	251	19·2	VII; R = Ph	227	11·2
		256	16·3		257	8·9
		282	4·5		268	9·6
		294 }	4·1		279	8·9
		304 }				
		324 }	3·2			
		343 }				
Imidine	I	251	15·9	VI	242	17·4
		258	14·5			
Dioxime from imidine	V	298	17·9	VIII; R = OH	228	16·5
Diphenylimine from imidine	IV	228	16·0			
		251	12·9			
		266	14·5			
		270	9·0			
		280	7·8			
		333	4·2			

* Inflexion.

at 691·5 and 532 mμ). At higher temperatures, particularly in the presence of an oxidising agent, pigment formation is faster and more complete. In a boiling mixture of dichlorobenzene and nitrobenzene, hexahydrophthalimidine gave a 53% yield of tetra*cyclo*hexenotetrazaporphin. The same pigment is formed when the imidine (which has no sharp point of melting or decomposition) is heated to 125°. These ready formations of the tetrazaporphin ring without the intervention of metallic reagents are noteworthy.

These and similar reactions are being studied further.

Endermann and Hans Fischer (*Annalen*, 1939, **538**, 183) prepared 2 : 5-diamino-3-ethyl-4-methylpyrrole (IX) from the corresponding diazide. The diamine, when heated, liberated ammonia and gave a pigment to which the tetraza*ætio*porphyrin structure was assigned. (The yield is not stated; the same pigment was made in 0·2% yield from the corresponding di*iso*cyanate.) This formulation is certainly correct, for we have shown that the light absorption of the Endermann–Fischer pigment is virtually identical with that of our compound for which the tetra*cyclo*hexenotetrazaporphin structure has been conclusively proved (*loc. cit.*, 1952). It is possible that the Endermann–Fischer precursor has the di-imine or the amino-imine rather than the diaminopyrrole structure (IX).



(IX)

Experimental

3 : 4 : 5 : 6-*Tetrahydrophthalimidine* (**Δ³-*Hexahydro*-1 : 3-*di*-*imino*isoindole**).—3 : 4 : 5 : 6-Tetrahydrophthalonitrile (4·70 g.) was heated in a stream of ammonia gas in boiling methanol (50 ml.) containing sodium (8 mg.). After 12 hr. the hot solution was filtered to remove tetra*cyclo*hexenotetrazaporphin (130 mg., 3%; identified spectroscopically), and the filtrate was

boiled with charcoal and refiltered. The filtrate was evaporated to dryness under reduced pressure and the residue was washed with cold ethyl acetate and then with ether. This left a pale brown solid (3·64 g., 69%). After two crystallisations from ethanol or preferably dimethylformamide 3 : 4 : 5 : 6-*tetrahydrophthalimidine* (I) was obtained as colourless plates (Found : C, 64·55; H, 7·7; N, 28·2. $C_8H_{11}N_3$ requires C, 64·4; H, 7·4; N, 28·2%). When the solid was heated, slight darkening began at about 165°, and rapid decomposition at 177—180°. The *picrate*, prepared in ethanol, had m. p. 202—204° (decomp.) (Found : C, 44·8; H, 4·4; N, 21·9. $C_{14}H_{14}O_7N_6$ requires C, 44·45; H, 3·7; N, 22·2%). A filtered solution of the base in ethanol was poured into ethereal hydrogen chloride, and the precipitate of *dihydrochloride monohydrate* was filtered off and washed with ether (Found : C, 39·7; H, 6·5; N, 17·3; Cl, 30·0. $C_8H_{11}N_3,2HCl,H_2O$ requires C, 40·0; H, 6·3; N, 17·5; Cl, 29·5%).

The free base (930 mg.) was set aside in cold water (10 ml.) for 18 hr. No apparent change occurred and the recovered solid was unchanged imidine, decomp. 175°. It was added to the filtrate which was then brought to the boil and cooled immediately. The solution was evaporated to dryness, and the residue was washed with boiling ether, to give Δ^8-hexahydro-1-imino-3-oxo*iso*indole (II; R = H) (440 mg.), m. p. 188—194° (decomp.), the mixed m. p. with material prepared as described below undepressed; the picrate had m. p. and mixed m. p. 188—189° (decomp.). The di-imine (164 mg.) was boiled with water (3 ml.) for 8 hr., and the solution was evaporated to dryness to give tetrahydrophthalimide, m. p. and mixed m. p. 168—170°.

2-Cyano-3 : 4 : 5 : 6-tetrahydrobenzamide (5·85 g.) (Ficken and Linstead, *loc. cit.*) was heated at 165—170° for 30 min., by which time the dark melt had almost completely resolidified. The product was boiled with ethanol (50 ml.), cooled, and filtered, to yield a pale brown solid, m. p. 193—198° (decomp.) (1·31 g.). After crystallisation from 2-ethoxyethanol (" Cellosolve ") Δ^8-*hexahydro*-1-*imino*-3-*oxoisoindole* was obtained colourless and had m. p. 200—202° (decomp.) (Found : C, 63·75; H, 6·8; N, 18·6. $C_8H_{10}ON_2$ requires C, 64·0; H, 6·7; N, 18·7%). The filtrate from the above preparation was evaporated to small volume and diluted with ethyl acetate, a second crop (1·05 g.) of slightly less pure material, m. p. 191—197°, being obtained. The *picrate*, crystallised from Cellosolve–ethanol, had m. p. 190—191° (decomp.) (Found : C, 44·5; H, 3·85; N, 18·5. $C_{14}H_{13}O_8N_5$ requires C, 44·3; H, 3·45; N, 18·5%). A solution of the keto-imine in ethanolic hydrogen chloride was evaporated to dryness under reduced pressure; the *hydrochloride*, crystallised from ethanol–ethyl acetate, had m. p. 250° (decomp.) (Found : N, 15·0; Cl, 19·8. $C_8H_{11}ON_2Cl$ requires N, 15·0 Cl, 19·0%).

The free keto-imine (II; R = H) (520 mg.) and hydroxylamine hydrochloride (350 mg.) were refluxed in "Cellosolve" (3 ml.) for 6 hr. The solvent was removed under reduced pressure and the residue was washed with water, to yield Δ^8-*hexahydro*-1-*hydroxyimino*-3-*oxoisoindole* (II; R = OH) (320 mg.), m. p. 245—246° (decomp.) after crystallisation from dilute ethanol (Found : C, 57·8; H, 6·3; N, 16·7. $C_8H_{10}O_2N_2$ requires C, 57·8; H, 6·1; N, 16·9%). The keto-imine (430 mg.), aniline (290 mg.), and " Cellosolve " (3 ml.) were refluxed for 6 hr. and the solvent was removed under reduced pressure. The residue was sublimed at 160°/0·3 mm. and the sublimate (350 mg.) was crystallised from aqueous ethanol. Δ^8-*Hexahydro*-1-*oxo*-3-*phenyliminoisoindole* (II; R = Ph) crystallised in pale yellow needles, m. p 128—129°, from light petroleum (b. p. 60—80°) (Found : C, 74·2; H, 6·4; N, 12·3. $C_{14}H_{14}ON_2$ requires C, 74·3; H, 6·2; N, 12·4%).

A solution of the imidine (I) (440 mg.) and hydroxylamine hydrochloride (490 mg.) in ethanol (5 ml.) was refluxed for 8 hr. On cooling, Δ^8-*hexahydro*-1 : 3-*dihydroxyiminoisoindole* (V) separated, and after crystallisation from dilute acetic acid had m. p. 252—253° (decomp.) (Found : C, 53·0; H, 6·4; N, 23·2. $C_8H_{11}O_2N_3$ requires C, 53·0; H, 6·1; N, 23·2%). A solution of the imidine (I) (290 mg.) and aniline (400 mg.) in ethanol (5 ml.) was refluxed for 40 hr. The solvent was removed and the residue was chromatographed on alumina in benzene; the yellow band was eluted and yielded Δ^8-*hexahydro*-1 : 3-*diphenyliminoisoindole* (IV) (360 mg.) as pale yellow needles, m. p. 146·5—147·5° after crystallisation from aqueous ethanol (Found : C, 79·45; H, 6·5; N, 13·9. $C_{20}H_{18}N_2$ requires C, 79·7; H, 6·35; N, 13·9%).

cis-*Hexahydrophthalimidine* (VI) (cis-*Octahydro*-1 : 3-*di-iminoisoindole*).—*cis*-Hexahydrophthalonitrile (6·7 g.) was dissolved in a solution of sodamide (3·9 g.) in dry formamide (35 ml.), and the solution left at room temperature for 2 days and then at 0° for 6 days. During this time the *imidine* (VI) crystallised as a hemihydrate in colourless needles, which were filtered off, washed with a little formamide, followed by ethyl acetate, and dried in a vacuum-desiccator (Found : C, 60·15; H, 8·5; N, 26·3. $C_8H_{12}N_2,\frac{1}{2}H_2O$ requires C, 60·0; H, 8·8; N, 26·2%). The yield was 5·2 g. (68%). The imidine was kept in a vacuum-desiccator over concentrated sulphuric acid, and slowly became blue. It did not melt, but began to become blue above 100°,

rapidly above 125°; the product in pyridine showed absorption bands due to tetra*cyclo*hexenotetrazaporphin (6270 and 5600 Å) (Ficken and Linstead, *loc. cit.*) and a hydrogenation product * (6915 and 5320 Å). The *imidine picrate*, prepared in absolute ethanol and crystallised from the same solvent in long yellow needles, had m. p. 209—210° (decomp.) (Found: C, 44·4; H, 4·5; N, 22·0. $C_{14}H_{16}O_7N_6$ requires C, 44·2; H, 4·2; N, 22·1%). The m. p. was depressed on admixture with 3 : 4 : 5 : 6-tetrahydrophthalimidine picrate to 194—196° (decomp.). The *dihydrochloride monohydrate* had m. p. 201—204° (decomp.) (Found: C, 39·1; H, 7·1; N, 17·4; Cl, 29·5. $C_8H_{13}N_3,2HCl,H_2O$ requires C, 39·7; H, 7·1; N, 17·4; Cl, 29·3%).

The imidine (210 mg.) readily dissolved in cold water. The solution soon smelt strongly of ammonia, and a white solid crystallised. This was filtered off after 4 hr. (76 mg.) and identified as *cis*-octahydro-1-imino-3-oxo*iso*indole (VII; R = H) by its m. p. and mixed m. p. 225—227° (decomp.). Evaporation of the filtrate at room temperature gave a further crop (92 mg.), m. p. 218—222° (decomp.). Both crops gave the same picrate, m. p. and mixed m. p. with the keto-imine picrate 204—206° (decomp.). The di-imine (320 mg.) was boiled with water for 6 hr., to yield *cis*-hexahydrophthalimide (290 mg.), m. p. 123—134°, raised to 135—137° by crystallisation from water.

Reaction of trans-*Hexahydrophthalonitrile with Sodamide.*—*trans*-Hexahydrophthalonitrile (2·41 g.) was added to sodamide (2·0 g.) in formamide (15 ml.), and the solution left for 4 days at room temperature and then at 0° for 8 days; the imidine (0·70 g.) was isolated as before and dried at room temperature at 10^{-5} mm. for 24 hr. This gave the anhydrous *imidine* (Found: C, 63·1; H, 8·6; N, 27·4. $C_8H_{13}N_3$ requires C, 63·5; H, 8·7; N, 27·8%). The picrate had m. p. 206—207° (decomp.) and mixed m. p. 208—209° with that of the di-imine from the *cis*-nitrile. The free base with cold water gave *cis*-octahydro-1-imino-3-oxo*iso*indole, m. p. 190—208° (decomp.) [picrate, m. p. 201—204° (decomp.) and mixed m. p. 202—205° (decomp.)].

*Tetra*cyclo*hexenotetrazaporphin from* cis-*Hexahydrophthalimidine.*—The imidine (VI) (615 mg.), *o*-dichlorobenzene (4·0 ml.), and nitrobenzene (1·0 ml.) were refluxed together. The solution became red immediately and then rapidly purple. Ammonia was copiously evolved and a blue solid was soon deposited. After 1 hr. the mixture was diluted with ethanol, and the solid was filtered off and washed with boiling ethanol. The yield of tetra*cyclo*hexenotetrazaporphin was 283 mg. (53%) (Found: N, 21·1. Calc. for $C_{32}H_{34}N_8$: N, 21·1%).

Reaction of the Imidine (VI) *with Bases.*—The imidine (530 mg.) and hydroxylamine hydrochloride (550 mg.) were refluxed in ethanol (5 ml.) for 22 hr. The solvent was removed and the residue was washed with a little cold water, to yield cis-1 : 3-*octahydrodihydroxyiminoisoindole* (VIII; R = OH) (250 mg.), m. p. 168—171° (decomp.) after crystallisation from ethyl acetate (Found: C, 52·2; H, 7·35; N, 22·8. $C_8H_{13}O_2N_3$ requires C, 52·4; H, 7·15; N, 22·9%).

The imidine (VI) (385 mg.) and aniline (505 mg.) in ethanol (5 ml.) were refluxed for 66 hr. The solution was filtered to remove a little pigment, and the filtrate was evaporated to dryness. The product was chromatographed in benzene on alumina, and the yellow band was eluted, to yield Δ^8-hexahydro-1 : 3-diphenyliminoisoindole (IV) (110 mg.), m. p. 134—138°; the m. p. was raised to 144—145° by crystallisation from aqueous ethanol, and was undepressed on admixture with authentic material.

Condensations with cis-*Octahydro*-1-*imino*-3-*oxoisoindole* (VII; R = H).—The keto-imine (370 mg.), hydroxylamine hydrochloride (220 mg.), and "Cellosolve" (5 ml.), refluxed for 16 hr., gave cis-*octahydro*-1-*hydroxyimino*-3-*oxoisoindole* (VII; R = OH), m. p. 216—218° (decomp.) after crystallisation from aqueous ethanol (Found: C, 57·4; H, 7·3; N, 16·6. $C_8H_{12}O_2N_2$ requires C, 57·1; H, 7·2; N, 16·7%). The same keto-imine (650 mg.), aniline (450 mg.), and "Cellosolve" (8 ml.) were refluxed for 36 hr., the solution was evaporated to dryness, and the residue was washed with ether. The yield of cis-*octahydro*-1-*oxo*-3-*phenyliminoisoindole* (VII; R = Ph) was 320 mg. and the m. p. after crystallisation from aqueous ethanol was 190—193° (Found: C, 73·8; H, 7·3; N, 12·65. $C_{14}H_{16}ON_2$ requires C, 73·65; H, 7·1; N, 12·3%).

We thank Imperial Chemical Industries Limited, Dyestuffs Division, for gifts of chemicals. Analyses were carried out in the microanalytical laboratory (Mr. F. H. Oliver), and spectrographic determinations in the spectrographic laboratory (Mrs. A. I. Boston), of the Department. We are grateful to Dr. J. A. Elvidge for helpful discussion.

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South Kensington, London, S.W.7. [*Received, March 30th*, 1955.]

* The hydrogenation of tetrazaporphins will be described in a later communication.

Heterocyclic Imines and Amines. Part V. The Imidine of αα′-Dimethylsuccinic Acid.*

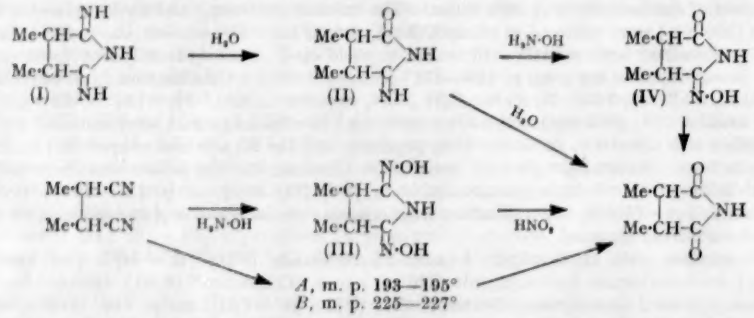
By R. P. Linstead and Margaret Whalley.

[Reprint Order No. 6283.]

DL-αα′-Dimethylsuccinonitrile reacts with ammonia in methanol at 150° to give *DL*-2 : 5-di-imino-3 : 4-dimethylpyrrolidine (dimethylsuccinimidine) (I). The degradation of (I) with water is described. It reacts normally with hydroxylamine hydrochloride to give a dihydroxyiminopyrrolidine, a stereoisomeride of which is one of the products from the reaction of hydroxylamine hydrochloride and dimethylsuccinonitrile. Dimethylsuccinimidine reacts abnormally with other primary amines. With aniline, dehydrogenation to the dimethylmaleic derivative (V) occurs; aniline hydrochloride gives the phenyliminoanilide (VIII); benzylamine and *cyclo*hexylamine give substituted imino-imides (X). Light-absorption data are given.

It has been shown that imidines are formed by adding ammonia to succinonitrile (Elvidge and Linstead, Part III, *J.*, 1954, 442) and hexahydrophthalonitrile (Ficken and Linstead *). This paper describes the symmetrically substituted *DL*-2 : 5-di-imino-3 : 4-dimethylpyrrolidine (dimethylsuccinimidine) (I) which is intermediate in structural type between these known imidines and is a valuable intermediate for the preparation of macrocyclic pigments.

DL-αα′-Dimethylsuccinonitrile (Linstead and Whalley, *J.*, 1954, 3722; the method described by Beech and Piggott, *J.*, 1955, 423, gives a mixture of *meso*- and *DL*-nitrile) reacts readily with methanolic ammonia to give good yields of dimethylsuccinimidine. This method resembles that used for succinimidine (Elvidge and Linstead, *loc. cit.*) and for 1 : 3-di-imino*iso*indoline (Elvidge and Linstead, Part I, *J.*, 1952, 5000). The temperature required



(150°) is higher than that previously used and careful control is essential: below 145° the yield of imidine is small whilst above 160° the product becomes increasingly difficult to work up. No dimethylsuccinimidine could be isolated after treatment of *DL*-αα′-dimethylsuccinonitrile with sodamide in formamide at room temperature or at 0° (cf. Part III), or by bubbling ammonia through a solution of the nitrile containing a trace of sodium (Part IV). No attempt was made to prepare the imidine from the less stable and less accessible *meso*-αα′-dimethylsuccinonitrile (Linstead and Whalley, *loc. cit.*) as the high temperature required for imidine formation would undoubtedly have caused inversion of configuration.

Dimethylsuccinimidine has no well-defined melting point, becomes blue at about 130°, and sinters at 140°. Hydrochloric acid hydrolyses it to *DL*-αα′-dimethylsuccinic acid. It therefore has the *DL*-configuration, which is known to be stable for cyclic derivatives of αα′-dimethylsuccinic acid (Linstead and Whalley, *loc. cit.*). Although fairly stable to atmospheric moisture, the imidine loses ammonia when its solution in cold water is allowed

* Part IV, preceding paper.

to stand. Evaporation of the water at room temperature then gives 5-imino-3 : 4-dimethylpyrrolid-2-one (II) which on further hydrolysis with boiling water gives *DL*-αα′-dimethylsuccinimide.

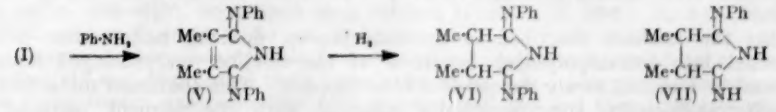
Dimethylsuccinimidine reacted in the expected manner with hydroxylamine hydrochloride in ethanol to give a dioxime (III*A*), m. p. 193—195°, identical with the product from the reaction of *DL*-αα′-dimethylsuccinonitrile with 2 mols. of hydroxylamine hydrochloride in boiling aqueous ethanol. Treatment of the dioxime (III*A*) at 0° with 2 mols. of sodium nitrite in dilute hydrochloric acid readily yielded *DL*-αα′-dimethylsuccinimide. Attempts at stepwise degradation of (III*A*) to the monoxime (IV) by reducing the proportion of sodium nitrite to less than 1 mol. led to *DL*-αα′-dimethylsuccinimide and hydroxylamine hydrochloride only. This suggested that the presumed intermediate monoxime (IV) was readily hydrolysed. The monoxime (IV) was prepared from the imino-imide (II) and hydroxylamine hydrochloride in boiling ethanol, and its rapid hydrolysis with dilute hydrochloric acid was confirmed.

A second dioxime (III*B*), m. p. 225—227°, was obtained from *DL*-αα′-dimethylsuccinonitrile and hydroxylamine hydrochloride in aqueous ethanol at 70°. This compound (III*B*) yielded *DL*-αα′-dimethylsuccinimide when treated with nitrous acid, whilst on irradiation in ethanol with ultraviolet light it gave the stable isomer (III*A*), m. p. 193—195°. These two dioximes are probably geometrical isomers of (III) for which three forms can be written (*syn-syn*, *syn-anti*, *anti-anti*). Tautomeric forms are also possible but seem to be excluded as the light absorptions of the two oximes are nearly identical. Indications of the existence of similar isomers have already been obtained in the succinic, 3 : 4 : 5 : 6-tetrahydrophthalic and hexahydrophthalic series (*locc. cit.*).

The reactions of dimethylsuccinimidine with water and with hydroxylamine conformed to those established for succinic and phthalic imidines. In its reaction with primary amines, however, dimethylsuccinimidine proved anomalous, and the symmetrically disubstituted product was not obtained. Three types of reaction occurred.

(a) ***With aniline.*** Dimethylsuccinimidine reacted with 2 mols. of aniline, very slowly at room temperature or in boiling ethanol, more rapidly in boiling propanol, or best at 90° with no solvent. The product was the unsaturated diphenylimine (V) which is a derivative of dimethylmaleic acid. The reaction is analogous to the dehydrogenation observed under similar conditions with *cis*-hexahydrophthalimidine (Ficken and Linstead, *loc. cit.*). The presence of the double bond is established by the light absorption and by the degradation to dimethylmaleimide. There was no evidence of the stepwise reaction with aniline, to give the monophenyl derivative, observed with 1 : 3-di-imino*iso*indoline (Clark, Elvidge, and Linstead, Part II, *J.*, **1953**, 3593) and with succinimidine (Part III). An attempt to prepare the monophenyl derivative (VII) by using 1 mol. of aniline gave the di-imine (V) alone.

Hydrogenation of the diphenylimine (V) over palladium–charcoal in ethanol gave the saturated diphenylimine (VI) which on hydrolysis yielded *DL*-αα′-dimethylsuccinimide.



Catalytic hydrogenation would be expected to give *cis*-addition of hydrogen to the ethylenic double bond as in the case of dimethylmaleimide which yields *meso*-αα′-dimethylsuccinimide (Linstead and Whalley, *loc. cit.*). It seems probable in the present case either that inversion of the labile *meso*-form occurs during the hydrolysis or that hydrogenation goes by an indirect process involving the nitrogen atoms. Rearrangement of the primary *N*-hydride would then yield the *C*-hydride in the stable *DL*-configuration.

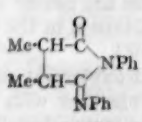
(b) ***With aniline hydrochloride.*** The reaction of aniline hydrochloride (2 mols.) with dimethylsuccinimidine was investigated as a possible route to the diphenylimine (VI), for it is known that 1 : 3-di-imino*iso*indoline with aniline hydrochloride gives 1 : 3-diphenylimino*iso*indoline hydrochloride. Reaction proceeded slowly at room temperature but

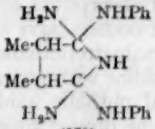
rapidly in boiling propanol, the only product isolated being the free base, 3 : 4-dimethyl-1-phenyl-5-phenyliminopyrrolid-2-one (VIII). The identity of the product was established by hydrolysis to *DL*-αα′-dimethyl-*N*-phenylsuccinimide. The light absorption was in agreement with structure (VIII). The formation of this compound, phenylated on the cyclic nitrogen atom, must involve a complex series of changes. Of possible courses for the reaction, the following seems the most likely: (*a*) formation from the imidine of the addition product (IX); (*b*) ring-opening and re-closing with elimination of ammonia; (*c*) hydrolysis of the imino-group. This conclusion will be correlated with other results in a later paper.

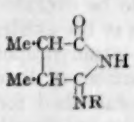
The *DL*-αα′-dimethyl-*N*-phenylsuccinimide required for comparison was prepared by the following route: mixed αα′-dimethylsuccinic acids ⟶ anhydrides ⟶ anilic acids ⟶ *N*-phenylimide. The product corresponded to that prepared by Bischoff and Voit (*Ber.*, **1890**, **23**, 643). Hydrolysis of the *N*-phenylimide with concentrated hydrochloric acid yielded *DL*-αα′-dimethylsuccinic acid only, indicating that the phenylimide was the *DL*-form.

Attempts to prepare the saturated diphenylimine (VI) by fusion of *DL*-αα′-dimethylsuccinonitrile with aniline hydrochloride failed (cf. succinonitrile and phthalonitrile; Part II).

(c) *With benzylamine and* cyclo*hexylamine.* Dimethylsuccinimidine reacts slowly with *cyclo*hexylamine at room temperature or in ethanol, or rapidly at 100° in the absence of solvent, to give a low yield of the substituted dimethylsuccinic imino-imide (X; R = C_6H_{11})


(VIII)


(IX)


(X)

which was isolated as the hydrochloride. Benzylamine reacts in the same way but more readily, even rapidly at room temperature, to give (X; R = CH_2Ph), also isolated as the hydrochloride. Both products gave *DL*-αα′-dimethylsuccinimide on hydrolysis.

Although dimethylsuccinimidine gives anomalous products with primary amines, the imino-imide (II) reacts normally with aniline and *cyclo*hexylamine, to give (X; R = Ph and C_6H_{11} respectively). These products are hydrolysed to *DL*-αα′-dimethylsuccinimide, indicating that dehydrogenation had not occurred.

The bases (V), (VI), (VIII), and (X; R = Ph, CH_2Ph, or C_6H_{11}) were readily hydrolysed to the corresponding imides with ethanolic dilute hydrochloric acid, but (VI) was known to be stable to hot dilute alkali for long periods. This behaviour corresponded to that of 1 : 3-diphenylimino*iso*indoline and, to a smaller extent, 1-imino-3-phenylimino*iso*indoline, which are stable to water and dilute alkali but are rapidly hydrolysed to phthalimide in the presence of dilute acid. Hydrolysis of the diphenylimine (VI) to the imide contrasted with that of 2 : 5-diphenyliminopyrrolidine (Part III) which in warm water gave succindianilide.

Like the imidines described in previous papers, dimethylsuccinimidine could be converted into tetrazaporphins. Solutions of the imidine, on prolonged boiling in propanol or butanol, slowly deposited a blue pigment. This contained metal-free octamethyltetrazaporphin, spectroscopically identical with the pigment prepared from dimethylfumaronitrile (Baguley, France, Linstead, and Whalley, *J.*, **1955**, 3521), together with a hydrogenation product of octamethyltetrazaporphin (main bands at 687 and 525 mμ). In boiling chlorobenzene–nitrobenzene, conversion of dimethylsuccinimidine into octamethyltetrazaporphin proceeded rapidly and in good yield. Dimethylsuccinimidine thus formed tetrazaporphins less readily than *cis*-hexahydrophthalimidine (Part IV) but much more easily than succinimidine (Elvidge and Linstead, following paper) from which metal-free tetrazaporphin could not be obtained directly. In one preparation of dimethylsuccinimidine during which the temperature exceeded 170° a good yield of macrocrystalline (unhydrogenated) octamethyltetrazaporphin was obtained.

The ultraviolet absorption data for dimethylsuccinimidine and its derivatives are

summarised in the Table. The spectra of compounds (I), (II), (III), (IV), (VI), and (X; R = Ph) closely resemble those of the corresponding derivatives of *cis*-hexahydrophthalimidine (Ficken and Linstead, *loc. cit.*) and of succinimidine (Elvidge and Linstead, Part III); that of the unsaturated diphenylimine (V) corresponds to that of the diphenyl derivative of 3 : 4 : 5 : 6-tetrahydrophthalimidine.

Light absorption of DL-αα'-*dimethylsuccinimidine and its derivatives in* EtOH.

Compound	Formula	$\lambda_{max.}$ (mμ)	$10^{-3}\varepsilon$
Imidine	(I)	237	17·8
Dioxime from imidine	(III*A*)	228	17·6
Dioxime from nitrile	(III*B*)	228	16·4
Diphenylimidine	(VI)	228	14·2
		282	16·8
Unsaturated diphenylimidine	(V)	228	15·3
		258 } 266 }	15·3
		328	7·4
		348	7·4
Imino-imide	(II)	227	27·0
Imino-imide oxime	(IV)	226	10·5
Phenylimino-imide	(X; R = Ph)	227	9·2
		269	11·5
*cyclo*Hexylimino-imide hydrochloride	(X; R = C_6H_{11}),HCl	250	6·5
Benzylimino-imide hydrochloride	(X; R = CH_2Ph),HCl	247	6·6
Phenylimino-anil	(VIII)	227	23·4
		265	5·0
N-Phenylimide	—	244	10·3

Experimental

DL-2 : 5-*Di-imino*-3 : 4-*dimethylpyrrolidine* (*Dimethylsuccinimidine*).—A solution of *DL*-αα'-dimethylsuccinonitrile (2·0 g.) in methanol (12 c.c.) was treated with liquid ammonia (8 c.c.), and the mixture heated in a sealed tube at 148° for 18 hr. The methanolic solution was filtered through charcoal and the residual oil triturated with ethyl acetate. After several hours a crystalline mass was obtained. Crystallisation from dimethylformamide–benzene gave pale yellow prisms of DL-2 : 5-*di-imino*-3 : 4 *dimethylpyrrolidine* (1·58 g., 69%), sinters at 140° after becoming blue at 130° (Found: C, 57·5; H, 8·8; N, 33·0. $C_6H_{11}N_3$ requires C, 57·6; H, 8·9; N, 33·6%). The *picrate* crystallised in yellow needles, m. p. 193—195° (decomp.), from ethanol (Found: C, 40·9; H, 4·1; N, 23·7. $C_{12}H_{14}O_7N_6$ requires C, 40·7; H, 4·0; N, 23·7%).

Hydrolysis. (*a*) Dimethylsuccinimidine (147 mg.) in water (1 c.c.) was refluxed for 1 hr. and the water evaporated under reduced pressure, giving *DL*-αα'-dimethylsuccinimide (123 mg., 82%), m. p. and mixed m. p. 104—106°.

(*b*) Dimethylsuccinimidine (300 mg.) was dissolved in cold water (3 c.c.). Ammonia evolution commenced after about 5 min. After 24 hr. the water was removed under reduced pressure. The sticky residue was crystallised from ethanol, giving colourless prisms of 5-*imino*-3 : 4-*dimethylpyrrolid*-2-*one* (178 mg., 59%), m. p. 173—176° (decomp.; darkening from 150°) (Found: C, 57·2; H, 8·1; N, 21·5. $C_6H_{10}ON_2$ requires C, 57·1; H, 8·0; N, 22·2%). The *picrate*, m. p. 208—210°, crystallised from ethanol (Found: C, 40·7; H, 4·0; N, 19·9. $C_{12}H_{13}O_8N_5$ requires C, 40·6; H, 3·7; N, 19·6%).

3 : 4-*Dimethyl*-5-*phenyliminopyrrolid*-2-*one*.—5-Imino-3 : 4-dimethylpyrrolid-2-one (274 mg.) and aniline (210 mg.) in propanol (2 c.c.) were refluxed for 6 hr. The propanol was removed and the sticky residue was crystallised from aqueous methanol and then from ethanol–light petroleum (b. p. 60—80°). It gave colourless prisms of 3 : 4-*dimethyl*-5-*phenyliminopyrrolid*-2-*one* (170 mg., 43%), m. p. 130—132° (Found: C, 71·6; H, 7·3; N, 14·5. $C_{12}H_{14}ON_2$ requires C, 71·3; H, 7·0; N, 13·9%).

The phenylimino-compound (49 mg.) was refluxed with 2N-hydrochloric acid (1 c.c.) and ethanol (1 c.c.), and the solvents were removed. The residue was sublimed under reduced pressure, giving *DL*-αα'-dimethylsuccinimide (26 mg., 84%), m. p. 103—105°.

5-cyclo*Hexylimino*-3 : 4-*dimethylpyrrolid*-2-*one Hydrochloride*.—5-Imino-3 : 4-dimethylpyrrolid-2-one (600 mg.) and *cyclo*hexylamine (1 g.) in propanol (10 c.c.) were refluxed for 6 hr. The propanol was removed under reduced pressure. The residue was dissolved in ether, and the ether solution dried (Na_2SO_4) and saturated with hydrogen chloride. The ether was removed and the solid crystallised from ethanol–light petroleum (b. p. 60—80°), giving

*5-cyclo*hexylimino-3 : 4-dimethylpyrrolid-2-one hydrochloride (27 mg., 3%), m. p. 248—250° alone or in admixture with the product from dimethylsuccinimidine.

5 - Hydroxyimino - 3 : 4 - dimethylpyrrolid - 2 - one.—5 - Imino-3 : 4 - dimethylpyrrolid - 2 - one (572 mg.), hydroxylamine hydrochloride (350 mg.), and anhydrous sodium carbonate (266 mg.) in absolute ethanol (8 c.c.) were refluxed for 24 hr. and the ethanol was removed. The residue was extracted with ethyl acetate, giving colourless prisms of *5-hydroxyimino-3 : 4-dimethylpyrrolid-2-one* (146 mg., 23%), m. p. 182—183° (Found : C, 51·1; H, 7·1; N, 19·3. $C_6H_{10}O_2N_2$ requires C, 50·7; H, 7·1; N, 19·7%). *DL-αα'*-Dimethylsuccinimide (10 mg.), m. p. 104—106°, was obtained from the mother-liquors.

The hydroxyimino-compound (27 mg.) was warmed at 65° for 15 min. with 0·01N-hydrochloric acid (0·5 c.c.). On cooling and evaporation, *DL-αα'*-dimethylsuccinimide (15 mg., 62%) separated.

2 : *5-Dihydroxyimino-3 : 4-dimethylpyrrolidines.*—(*a*) A solution of *DL-αα'*-dimethylsuccinonitrile (2·0 g.), hydroxylamine hydrochloride (2·8 g., 2 mols.), and sodium carbonate (1·4 g.) in ethanol (16 c.c.) and water (16 c.c.) was refluxed for 16 hr. Traces of metal-free octamethyltetrazaporphin were formed during the early stages of the reaction. The ethanol and water were removed under reduced pressure and the dried solid extracted with ethyl acetate.

2 : *5-Dihydroxyimino-3 : 4-dimethylpyrrolidine* (III*A*) (1·6 g., 56%), m. p. 193—196° (decomp.), was obtained as colourless prisms from ethyl acetate (Found : C, 46·0; H, 7·1; N, 26·2. $C_6H_{11}O_2N_3$ requires C, 45·9; H, 7·1; N, 26·7%).

(*b*) Dimethylsuccinimidine (100 mg.), hydroxylamine hydrochloride (112 mg.), and sodium carbonate (86 mg.) in absolute ethanol (6 c.c.) were refluxed for 24 hr. and the solvent was then removed. The residue crystallised from ethyl acetate, giving 2 : 5-dihydroxyimino-3 : 4-dimethylpyrrolidine (89 mg., 71%), m. p. 193—196° (decomp.) alone and in admixture with the above product from *DL-αα'*-dimethylsuccinonitrile (Found : C, 45·8; H, 7·1%).

(*c*) *DL-αα'*-Dimethylsuccinonitrile (1·0 g.), hydroxylamine hydrochloride (0·71 g., 1 mol.), anhydrous sodium carbonate (0·4 g.), ethanol (8 c.c.), and water (8 c.c.) were heated at 70° overnight, and the ethanol and some of the water removed. The remaining solid crystallised from ethyl acetate, giving 2 : *5-dihydroxyimino-3 : 4-dimethylpyrrolidine* (III*B*), m. p. 225—227° (decomp.) (Found : C, 46·2; H, 7·2; N, 27·1%).

Irradiation of an ethanolic solution of this dioxime with ultraviolet light for 6 hr. gave the isomer (III*A*), m. p. 193—196°.

Degradation of 2 : *5-Dihydroxyiminopyrrolidines.*—(a) *The isomer* (III*A*). (i) The dioxime (248 mg.) was dissolved in warm water (20 c.c.), and the solution cooled in ice. Sodium nitrite (218 mg.) was added, followed by 2N-hydrochloric acid (2·1 c.c.) in portions. After 5 min. the water was removed under reduced pressure and the residue sublimed (156 mg., 88%); it had m. p. 101—104° alone and when mixed with *DL-αα'*-dimethylsuccinimide.

(ii) The dioxime (200 mg.) was treated with sodium nitrite (34 mg.) and 2N-hydrochloric acid as above. The solid obtained on evaporation of the solution was extracted with ethanol, giving hydroxylamine hydrochloride (14 mg., 17%), m. p. and mixed m. p. 150—151°, and *DL-αα'*-dimethylsuccinimide (87 mg., 54%), m. p. 104—106°.

(iii) The compound (100 mg.) was hydrolysed with concentrated hydrochloric acid, giving *DL-αα'*-dimethylsuccinic acid (75 mg., 92%), m. p. 123—127°.

(b) *The isomer* (III*B*). This form (100 mg.) was treated with sodium nitrite (88 mg.) and 2N-hydrochloric acid (1 c.c.) as above, giving *DL-αα'*-dimethylsuccinimide (74 mg., 93%), m. p. and mixed m. p. 105—107°.

3 : *4-Dimethyl-2 : 5-diphenylimino-Δ³-pyrroline.*—(*a*) A solution of dimethylsuccinimidine (610 mg.) and aniline (910 mg.) in propanol was refluxed for 20 hr. The propanol was removed under reduced pressure, the residue chromatographed (alumina–benzene), and the eluate evaporated. The sticky residue was crystallised several times from 50% aqueous ethanol, giving yellow needles of 3 : *4-dimethyl-2 : 5-diphenylimino-Δ³-pyrroline* (190 mg., 14%), m. p. 98—100° (Found : C, 78·5; H, 6·4; N, 15·6. $C_{18}H_{17}N_3$ requires C, 78·5; H, 6·2; N, 15·3%).

(*b*) Dimethylsuccinimidine (200 mg.) and aniline (300 mg.) were warmed at 90° overnight and the mixture was worked up as above, giving the same diphenylimine (50 mg., 12%).

The diphenylimine was recovered unchanged after refluxing for 4 hr. with 2N-sodium hydroxide.

The dimethyldiphenyliminopyrroline (100 mg.) was refluxed with 2N-hydrochloric acid (2 c.c.) and ethanol (1 c.c.) for 10 min., the solvents were removed, and the residue was crystallised from water, giving dimethylmaleimide (32 mg., 70%), m. p. and mixed m. p. 118—119°.

Hydrolysis of Phenyliminoisoindolines.—(*a*) 1-Imino-3-phenyliminoisoindoline was unchanged after being boiled for 5 min. with water or for 10 min. with 0·1N-sodium hydroxide (10 c.c.) and ethanol (10 c.c.). (*b*) 1 : 3-Diphenyliminoisoindoline (0·1 g.), 0·1N-sodium hydroxide (10 c.c.), and ethanol (10 c.c.) were refluxed for 10 hr. Addition of a few drops of concentrated hydrochloric acid gave a bright yellow solid, which, crystallised from glacial acetic acid, had m. p. 285° alone or in admixture with the authentic hydrochloride. (*c*) The base (0·1 g.) was unchanged after being refluxed overnight with 40% sodium hydroxide solution (10 c.c.).

3 : 4-*Dimethyl*-2 : 5-*diphenyliminopyrrolidine.*—3 : 4-Dimethyl-2 : 5-diphenylimino-Δ^3-pyrroline (281 mg.) was hydrogenated over 5% palladium–charcoal in ethanol, and the catalyst and the solvent were removed. The residue crystallised from aqueous ethanol, giving colourless prisms of 3 : 4-*dimethyl*-2 : 5-*diphenyliminopyrrolidine hemihydrate* (203 mg., 72%), m. p. 101—103° (Found : C, 75·8; H, 7·4; N, 15·1. $C_{18}H_{19}N_3,\frac{1}{2}H_2O$ requires C, 75·5; H, 7·1; N, 14·7%).

This diphenylimine (61 mg.) was refluxed with 2N-hydrochloric acid (1 c.c.) and ethanol (0·5 c.c.) for 10 min. Evaporation of the solvent and sublimation of the residue gave *DL*-αα′-dimethylsuccinimide (21 mg., 75%), m. p. and mixed m. p. 101—106°.

1 : 3-*Diphenyliminoisoindoline Hydrochloride.*—1 : 3-Di-iminoisoindoline (250 mg.) and aniline hydrochloride (450 mg.) were refluxed in propanol for 24 hr. and the propanol removed under reduced pressure. The remaining solid was crystallised several times from glacial acetic acid, giving 1 : 3-diphenyliminoisoindoline hydrochloride (320 mg., 56%), m. p. and mixed m. p. 275—278°.

3 : 4-*Dimethyl*-1-*phenyl*-5-*phenyliminopyrrolid*-2-*one.*—Dimethylsuccinimidine (250 mg.) and aniline hydrochloride (520 mg.) were refluxed in propanol for 6 hr. The precipitated ammonium chloride was removed and the solvent evaporated. The sticky residue was crystallised from aqueous ethanol, giving colourless needles of 3 : 4-*dimethyl*-1-*phenyl*-5-*phenyliminopyrrolid*-2-*one* (117 mg., 22%), m. p. 107—109° (Found : C, 77·7; H, 6·5; N, 10·3. $C_{18}H_{18}ON_2$ requires C, 77·7; H, 6·5; N, 10·1%).

Hydrolysis of the substance (63 mg.) in ethanol (1 c.c.) and 2N-hydrochloric acid (2 c.c.) yield *DL*-αα′-dimethyl-*N*-phenylsuccinimide (25 mg., 55%), m. p. and mixed m. p. 126—127°.

DL-αα′-*Dimethyl*-N-*phenylsuccinimide.*—A mixture of the stereoisomeric αα′-dimethylsuccinic acids (5 g.) was refluxed with acetyl chloride (20 c.c.) for 45 min. and the mixture cooled and filtered. The acetyl chloride and acetic acid were removed under reduced pressure, giving a mixture of *meso*- and *DL*-αα′-dimethylsuccinic anhydride (3·54 g., 81%), m. p. 60—75°. The mixture was refluxed with aniline (2·64 g.) and ethanol (25 c.c.) for 6 hr., the ethanol evaporated, and the residue crystallised several times from aqueous ethanol, giving *meso*- and *DL*-αα′-dimethylsuccinanilic acid (3·90 g., 64%), m. p. 151—154° (Bone and Sprankling, *J.*, 1899, **75**, 861, give m. p. 169—171° for the *meso*- and 135—136° for the *DL*-anilic acid) (Found : C, 65·9; H, 7·1; N, 6·6. Calc. for $C_{12}H_{15}O_3N$: C, 65·2; H, 6·8; N, 6·3%).

Hydrolysis of this mixture of anilic acids (200 mg.) with concentrated hydrochloric acid (2·5 c.c.) yielded a mixture of *meso*- and *DL*-αα′-dimethylsuccinic acid (127 mg., 96%), m. p. 145—150°.

The mixture of αα′-dimethylsuccinanilic acids (1·0 g.) was heated at 150° for 10 min., the residue sublimed under reduced pressure, and the sublimate crystallised from ethanol, giving *DL*-αα′-dimethyl-*N*-phenylsuccinimide (0·87 g., 96%), m. p. 126—127° (Bischoff and Voit, *Ber.*, 1890, **23**, 643, give m. p. 126—127°) (Found : C, 70·7; H, 6·4; N, 7·2. Calc. for $C_{12}H_{13}O_2N$: C, 70·9; H, 6·4; N, 6·9%).

Hydrolysis of *DL*-αα′-dimethyl-*N*-phenylsuccinimide (117 mg.) with concentrated hydrochloric acid (82 mg., 97%), m. p. 125—127° alone and in admixture with *DL*-αα′-dimethylsuccinic acid.

The anil was recovered unchanged after being refluxed for 10 min. with ethanol and 2N-hydrochloric acid (1 : 2).

5-cyclo*Hexylimino*-3 : 4-*dimethylpyrrolid*-2-*one Hydrochloride.*—Dimethylsuccinimidine (500 mg.) and *cyclo*hexylamine (800 mg.) were heated on the steam-bath overnight (evolution of ammonia occurred slowly at room temperature). The product was dissolved in ether, and the solution washed with water and dried (Na_2SO_4). The oil obtained after evaporation of the ether was dissolved in ethanol (1 c.c.) and dry ether (10 c.c.), and the solution saturated with hydrogen chloride. The *pyrrolidone hydrochloride* separated (47 mg., 9%), having m. p. 248—250° (decomp.) after crystallisation from ethanol–light petroleum (b. p. 60—80°) (Found : C, 59·0; H, 8·4; N, 11·5; Cl, 14·7. $C_{12}H_{21}ON_2Cl$ requires C, 58·8; H, 8·6; N, 11·5; Cl, 14·5%).

Hydrolysis of the hydrochloride (41 mg.) with boiling ethanol (0·5 c.c.) and 2N-hydrochloric acid (0·5 c.c.) gave *DL-αα'*-dimethylsuccinimide (11 mg., 52%), m. p. 103—105°.

5-Benzylimino-3 : 4-dimethylpyrrolid-2-one Hydrochloride.—Dimethylsuccinimidine (500 mg.) and benzylamine (1 g.) were heated on the steam-bath overnight (evolution of ammonia at room temperature was rapid) and the residue dissolved in ether. The ether solution was washed with water and dried (Na_2SO_4), and evaporated. The sticky residue was dissolved in ether (10 c.c.), the solution saturated at 0° with hydrogen chloride, and the ether removed. A colourless solid, m. p. 218—227°, separated and gave, on recrystallisation from ethanol, *5-benzylimino-3 : 4-dimethylpyrrolid-2-one hydrochloride* (173 mg., 17%), m. p. 236—238° (Found : C, 61·5; H, 6·6; N, 10·9; Cl, 13·9. $C_{13}H_{17}ON_2Cl$ requirss C, 61·8; H, 6·8; N, 11·1; Cl, 14·0%).

The hydrochloride (37 mg.) was refluxed for 15 min. with ethanol (0·5 c.c.) and 2N-hydrochloric acid (0·5 c.c.), and the solvents were removed under reduced pressure. Sublimation of the residue gave *DL-αα'*-dimethylsuccinimide (9 mg., 48%).

Octamethyltetra-azaphorphin.—Dimethylsuccinimidine (150 mg.) was refluxed with chlorobenzene (5·5 c.c.) and nitrobenzene (4·5 c.c.) for 5 hr. The mixture was diluted with methanol, and the solid was filtered off and crystallised from chlorobenzene, giving prisms of metal-free octamethyltetra-azaporphin (59 mg., 45%) (Found : C, 67·2; H, 6·1; N, 25·5. Calc. for $C_{24}H_{26}N_8$: C, 67·6; H, 6·2; N, 26·3%) ($\lambda_{max.}$ in chlorobenzene : 6270, 5560 Å; cf. Baguley, France, Linstead, and Whalley, *J.*, 1955, 3521).

Microanalyses and spectrographic determinations were made in the microanalytical (Mr. F. H. Oliver) and the spectrographic (Mrs. A. I. Boston) laboratories of this Department.

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Conjugated Macrocycles. Part XXVII. The Formation of Tetrazaporphins from Imidines. Tribenzotetrazaporphin.*

By J. A. Elvidge and R. P. Linstead.

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Condensations between imidines (with elimination of ammonia) are discussed. Self-condensation of 4 mols. of either a saturated or an unsaturated (or aromatic) imidine can yield only compounds containing the tetrazaporphin skeleton at unfavourable hydrogenation levels, and so can yield tetrazaporphins only through supplementary oxidation–reduction processes. The condensation between imidines at different hydrogenation levels, however, can yield directly tetrazaporphins or their di- or tetrahydro-derivatives. The preferred reaction will be between 3 mols. of unsaturated and 1 mol. of saturated imidine. There is distinct evidence, experimentally, that these guiding principles operate.

Metal-free phthalocyanine is formed by heating di-imino*iso*indoline, in appreciable yields only in the presence of hydrogen donors. Heating the imidine with metal salts or metals gives the metal phthalocyanines under mild conditions.

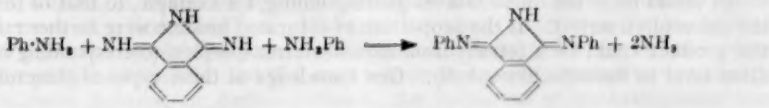
Magnesium tetrazaporphin is prepared in low yield by heating succinimidine with magnesium formate. The metal-free pigment could not be obtained directly from succinimidine.

The condensation of succinimidine with di-imino*iso*indoline (in the absence of metals) readily gives a mixture of tetrazaporphin pigments, containing mainly phthalocyanine and a new blue compound, tribenzotetrazaporphin, isolated by chromatography. Its structure follows from the elementary analysis, the light absorption spectrum, and oxidative degradation.

It has been shown that the newly discovered imidines (Elvidge and Linstead, *J.*, 1952, 5000; Clark, Elvidge, and Linstead, *J.*, 1953, 3593; Elvidge and Linstead, *J.*, 1954, 442;

* Part XXVI, *J.*, 1955, 3521.

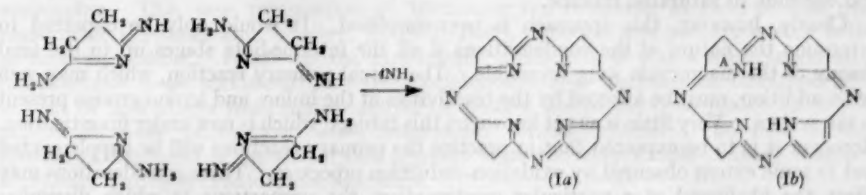
Ficken and Linstead, *J.*, 1955, 3525; Linstead and Whalley, *J.*, 1955, 3530) react readily with 2 mols. of a primary base with elimination of ammonia. This reaction involves both of the extranuclear imino-groups (real or potential) of the imidine and for our present purpose can be exemplified by the reaction between di-imino-*iso*indoline and aniline:



The process occurs alike with imidines derived from saturated, unsaturated, or aromatic 1 : 2-dinitriles.

Imidines can be represented as imino-amino-structures or as di-imines. In addition, imidines of the succinic series might exist or react as 2 : 5-diaminopyrroles. Imidines could thus conceivably provide *both* components in a process of the above kind. Elimination of ammonia between molecules of the same imidine or of dissimilar imidines could theoretically lead to products of two main types, either linear polycondensation products or macrocycles. The imidine from phthalic acid (1 : 3-di-imino*iso*indoline) reacts very easily with suitably oriented diamines to give cross-conjugated macrocycles containing four heterocyclic corner units (Elvidge and Linstead, *J.*, 1952, 5008; Clark, Elvidge, and Linstead, *J.*, 1954, 2490). This illustrates, experimentally, the readiness with which imidines yield *syn*-condensation products and suggests that they might self-condense to give tetrapyrrolic macrocycles of the tetrazaporphin type.

There are, however, complications arising from the hydrogenation level of the system. This can be exemplified by the hypothetical self-condensation of succinimidine, represented below as an interaction of four molecules in the imino-amine form; the first macrocyclic product would be the octahydride (I*a*) of a dehydrotetrazaporphin or its tautomer (I*b*), the hexahydride of tetrazaporphin. Compound (I*a*) contains an inner ring which, although conjugated, is of a type which appears to be unstable. Thus, phthalocyanines and tetrazaporphins show no tendency to lose their two central hydrogen atoms by

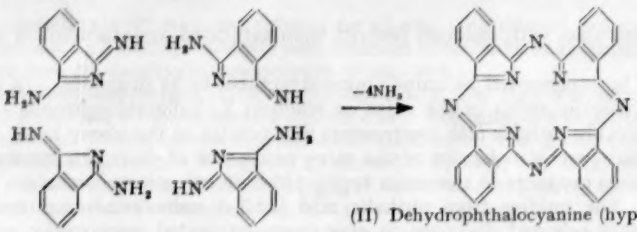


dehydrogenation (Linstead and Weiss, *J.*, 1950, 2981), and the same appears to be true of porphyrins. In compound (I*b*) the formal conjugation is broken at ring A. There are reasons, therefore, to expect that these substances would have a low degree of stability and would not be formed with the same facility as the tetrazaporphins themselves.

The self-condensation of unsaturated or aromatic imidines (which for the present purpose are formally equivalent) can be exemplified by 1 : 3-di-imino*iso*indoline. Four mols. of this, without oxidation–reduction, could only yield a macrocycle at the unfavourable dehydrotetrazaporphin hydrogenation level (II). This can be formulated as generalisation (i), that *self-condensation of imidines of* 1 : 2-*dicarboxylic acids can yield only compounds containing the tetrazaporphin skeleton at comparatively unfavourable hydrogenation levels, and can only yield tetrazaporphins themselves through supplementary oxidation–reduction processes.*

The equivalent generalisations would obviously hold for condensations between dissimilar imidines at the same hydrogenation level. If, however, we examine the condensation between imidines at different hydrogenation levels, the case is altered. Three mols. of an unsaturated or aromatic imidine can react with one mol. of a saturated imidine to

give a macrocycle at the fully " aromatic " tetrazaporphin level. Thus the reaction between di-imino*iso*indoline and succinimidine (written below as diaminopyrrole) could take the course illustrated, to give (III). This is not, however, the only possible mode of reaction between these substances. If the proportion of saturated to aromatic imidine were raised to 2 : 2, then the formation of a dibenzotetrazaporphin could be envisaged, which would be at the dihydro-level (corresponding, for example, to that of the chlorins of the chlorophyll series). If the proportion of saturated imidine were further raised to 3 : 1, the product could be a tetrahydromonobenzotetrazaporphin (corresponding in hydrogenation level to bacteriochlorophyll). Our knowledge of these types of structure, although



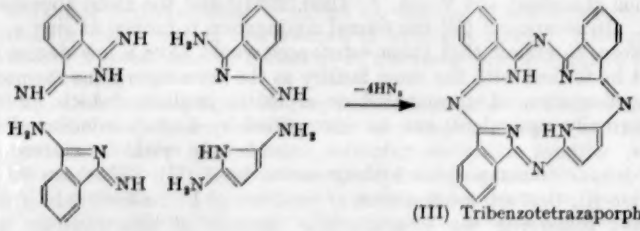
(II) Dehydrophthalocyanine (hypothetical)

very incomplete, suggests that, while neither of these systems would be as stable as the fully " aromatic " tetrazaporphin state, both would have a reasonable stability. These two modes of combination may therefore be possible, if less favourable than that leading to tribenzotetrazaporphin (III).

These considerations yield generalisation (ii), that *condensation between (dissimilar) imidines at different hydrogenation levels can yield, without oxidation–reduction processes, either tetrazaporphins themselves or their di- or tetra-hydro-derivatives.*

If postulates (i) and (ii) were correct and no other factors operated reasonable corollaries would be : (iii) dissimilar imidines at different hydrogenation levels will combine preferentially one with another, rather than by autocondensation; and (iv) the preferred mode of condensation will be that involving three mols. of unsaturated (or aromatic) imidine and one mol. of saturated imidine.

Clearly, however, this approach is over-simplified. It would only be expected to determine the nature of the condensations if all the intermediate stages up to the final closure of the macrocycle were reversible. The actual primary reaction, which may well be an addition, must be affected by the reactivities of the imino- and amino-groups present in the system. Very little is as yet known on this subject, which is now under investigation. Moreover it is to be expected that in practice the primary reactions will be supplemented and to some extent obscured by oxidation–reduction processes. These considerations may affect the likelihood of a particular condensation, the proportions in which dissimilar



(III) Tribenzotetrazaporphin.

imidines will combine, the state of hydrogenation of the product, and even the occurrence or absence of self-condensation of a single imidine under a particular set of reaction conditions. The position is further complicated as each intermediate stage may become involved in oxidation–reduction processes. Reversible deaminations (imidine $\rightleftharpoons$ dinitrile + NH_3) are also possible complications.

We have now made a preliminary experimental exploration of this field. In summary, we find: first, that mixtures of imidines can condense to give tetrapyrrolic macrocycles without the intervention of metallic reagents; secondly, that there is distinct evidence of the operation of the principles formulated above, which are however to some extent obscured by oxidation–reduction.

The main substances examined were succinimidine and di-imino*iso*indoline.* Their self-condensations were first examined. When heated alone, di-imino*iso*indoline melted at about 196°, and then evolved ammonia. This was due mainly to a reversal of imidine formation, for phthalonitrile sublimed and only a trace of a green pigment was produced. In boiling ethanol, butanol, or 2-ethoxyethanol, the formation of phthalocyanine was negligible. The main products in the last case were ammonia and tricyanocyaphenine, the cyclic trimeride of phthalonitrile (Dent and Linstead, *J.*, 1938, 715; Linstead and Lowe, *J.*, 1934, 1022). The presence of hydrogen donors greatly improved the formation of phthalocyanine. Thus in boiling butanol containing succinonitrile, di-imino*iso*indoline gave a 34% yield of phthalocyanine, whilst a boiling solution of di-imino*iso*indoline in tetralin gave 45% of phthalocyanine quite rapidly. In contrast, in nitrobenzene (a dehydrogenating agent) at the same temperature virtually no phthalocyanine was formed.

These processes are noteworthy as providing mild methods for the preparation of phthalocyanine in the absence of metals. None of them is as efficient as the equivalent reaction between the same imidine and metal salts. For example, in hot formamide with nickel acetate, the imidine almost at once forms nickel phthalocyanine quantitatively. Less effective was copper powder in boiling butanol, which gave from the imidine a 24% yield of copper phthalocyanine in 5 min.

The conversion of succinimidine into tetrazaporphin proved as difficult as expected. None at all could be detected by the use of purely organic media, although unstable coloured products of other types were obtained. However, Mr. J. S. Fitt found that traces of magnesium tetrazaporphin were formed by heating succinimidine with magnesium acetate in nitrobenzene, and with magnesium formate in boiling 2-ethoxyethanol alone or mixed with nitrobenzene. The last combination of reagents was most reliable, and from 1-g. quantities of succinimidine the average yield of magnesium tetrazaporphin was 3%. The pigment was identified spectroscopically and by conversion into metal-free tetrazaporphin. This new preparation of tetrazaporphin is inferior in yield to that from maleinitrile (Linstead and Whalley, *J.*, 1952, 4839), although it is perhaps a little better in time and labour. It affords the magnesium pigment in 3 stages from acrylonitrile (acrylonitrile ⟶ succinonitrile ⟶ succinimidine ⟶ magnesium tetrazaporphin) instead of in 4 stages from maleic anhydride (maleic anhydride ⟶ maleic ester ⟶ maleamide ⟶ maleinitrile ⟶ magnesium tetrazaporphin). The new method provides a synthesis of an azaporphin pigment from the very simple primary reagents, acetylene, hydrogen cyanide, and ammonia.

Mixed Condensation: *The Formation of Tribenzotetrazaporphin.*—The elimination of ammonia proceeded more readily from a mixture of succinimidine and di-imino*iso*indoline than from either component alone. When equivalent quantities were heated together in boiling butanol the two imidines were converted almost completely into a dark insoluble product. This was made up mainly of a charcoal-like insoluble poly-condensation product together with about 20% of a chlorobenzene-soluble blue pigment. The pigment was largely composed of phthalocyanine (main bands at 698 and 665 mμ) and of a new blue compound (main bands at 675 and 594 mμ) subsequently shown to be tribenzotetrazaporphin. There were also traces of a third pigment (main bands at 640 and 590 mμ) which may be a related tetrazaporphin. The first extracts of the crude reaction product also yielded pigment with bands at 752 and 721 mμ but this was labile and did not survive the working up. There is little doubt that it was a hydro-derivative. When the molar proportion of succinimidine to aromatic imidine was raised to 3 : 1, the yield of dark insoluble product was again high but extraction yielded only about 2% of mixed macrocyclic pigments (bands at 720, 698, 675, 640, 590, 548 mμ).

* Preliminary examination of the formation of pigments from 3 : 4 : 5 : 6-tetrahydro- and hexahydrophthalimidine (Ficken and Linstead, *loc. cit.*) gives results in general agreement.

Reaction in boiling butanol of the two imidines in the molar proportion of 1 of succinimidine to 3 of di-imino*iso*indoline, however, gave a more satisfactory product, 32% of mixed pigment being obtained from the crude material. This process was made the basis of further work.

Purification of tribenzotetrazaporphin. This is time-consuming. Although the tribenzo-pigment is soluble in benzene and chlorobenzene in which its tetrabenzo-analogue (phthalocyanine) is ordinarily insoluble, traces of phthalocyanine are carried through and can be separated only by chromatographic procedures. These are arduous because the solutions are (necessarily) so very dilute. The essential steps are: (i) Reduction of the phthalocyanine content by repeated extraction with chlorobenzene (the phthalocyanine largely remains in the residues). (ii) Removal of phthalocyanine from the extracts by chromatography on tartaric acid or mucic acid, two novel adsorbents. (iii) Final purification of tribenzotetrazaporphin from traces of a related (? di- or mono-benzo) pigment by chromatography on kieselguhr.

The product of stage (i) already gave correct elementary analyses for tribenzotetrazaporphin, $C_{28}H_{16}N_8$. The light absorption curve of its chlorobenzene solution, however, showed the presence of traces of phthalocyanine and this was confirmed by chromatography on alumina or mucic acid. For stage (ii) the preferred procedure was, first, chromatography of a chlorobenzene solution on tartaric acid: phthalocyanine came through rapidly, followed by the new pigment. This was taken up in benzene and rechromatographed on tartaric acid, which eliminated the last traces of phthalocyanine. At stage (iii), elution from the kieselguhr with chlorobenzene removed the tribenzotetrazaporphin and left a persistent contaminant as a small mauve band.

Properties of tribenzotetrazaporphin. The new compound is intermediate in properties between phthalocyanine and tetrazaporphin (Linstead and Whalley, *J.*, 1952, 4839). It crystallises from its vividly royal-blue solutions in small needles with a purple reflex. It decomposes without melting at about 400°. Sublimation (at 350°/15 mm. in nitrogen) was not a useful method of purification but gave a most interesting result, some phthalonitrile and phthalocyanine being formed. Evidently the phthalocyanine was derived from thermal breakdown of the tribenzo-compound.

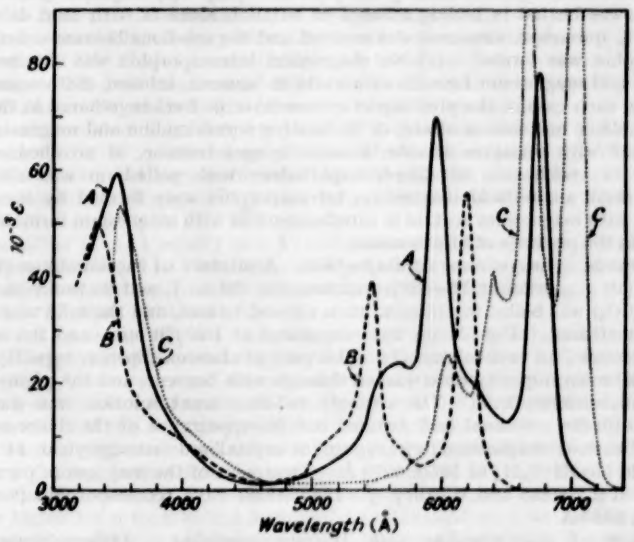
The solubility of tribenzotetrazaporphin, although low, is considerably greater than that of phthalocyanine. A wide range of solvents (for example, benzene, anisole, pyridine, morpholine) dissolve it to the extent of 1—10 mg. per l. The solutions so obtained dissolve phthalocyanine to an appreciable extent, although it is quite insoluble in the pure solvents. The solutions of the mixed pigments are considerably greener than those of the pure tribenzo-compound and show the characteristic absorption bands of both components. This mutual solubility effect may be due to association between the two kinds of molecules, this being facilitated by their similarities in shape and size. The two pigments also form mixed crystals. Solutions of tribenzotetrazaporphin have a dull red fluorescence in ultraviolet light, considerably weaker than the rose-red fluorescence of tetrazaporphin itself. Solutions of phthalocyanine in chloronaphthalene show no ultraviolet fluorescence.

The light absorption of tribenzotetrazaporphin in chlorobenzene over the range 320—1000 mμ is recorded in the Figure, together with the curves for tetrazaporphin and phthalocyanine. Comment is reserved until the collection of corresponding data on the metallic derivatives has been completed.

Structure of tribenzotetrazaporphin. The empirical formula is $C_7H_4N_2$. The compound forms metallic derivatives (Elvidge, Golden, and Linstead, work in progress) of the general composition $C_{28}H_{14}N_8M$ where M is a bivalent, tetraco-ordinate metal. Hence the parent compound can be presumed to be $C_{28}H_{14}N_8 \cdot H_2$. This corresponds to an aggregate of three phthalonitrile units ($C_8H_4N_2$) together with one maleinitrile unit ($C_4H_2N_2$) and the two replaceable atoms of hydrogen. The presence of the last-named is confirmed by quantitative oxidation with ceric sulphate, by which the pigment is destroyed with the consumption of 1 atom of oxygen (cf. Dent, Linstead, and Lowe, *J.*, 1934, 1036). The light absorption at the long-wave end of the visible region is of the general tetrazaporphin type, and the first ultraviolet band resembles closely in position and intensity the similar bands of known tetrazaporphins. This evidence leads to the tribenzotetrazaporphin

structure, one canonical form of which is shown as (III). The evidence has been completed by comparison of the oxidation of the new pigment with that of phthalocyanine. For this purpose we used hydrogen peroxide in sulphuric acid solution. With this reagent almost the theoretical amount of the phthalic residues (corresponding to four corners of the molecule) was isolated from phthalocyanine, 80% being in the form of phthalimide, the rest as phthalic acid. Tribenzotetrazaporphin, on the other hand, yields phthalic derivatives to an extent corresponding to only three corners of the molecule (82% as phthalimide, the rest as phthalic acid). No definite fragment was isolated corresponding to the simple pyrrole corner. This was not surprising as virtually no maleic derivative could be isolated from the oxidation of tetrazaporphin itself (Linstead and Whalley, *loc. cit.*). The phthalic acid from the oxidation of tribenzotetrazaporphin was accompanied by some gum, and this presumably corresponds with the degradation of the pyrrole fragment.

Absorption of (A) *tribenzotetrazaporphin (in chlorobenzene),* (B) *tetrazaporphin (in chlorobenzene), and* (C) *phthalocyanine (in chloronaphthalene).*



Experimental

Extractions and extractive crystallisations were performed with an all-glass apparatus similar to that described by Barrett, Dent, and Linstead (*J.*, 1936, 1726).

Self-condensation of 1 : 3-*Di-iminoisoindoline.*—(a) *Exploratory work.* (i) Di-imino*iso*indoline (0·5 g.) was heated in a Monax test tube. The imidine melted, became green, bubbled, and evolved ammonia rapidly, and up the sides of the tube phthalonitrile (40 mg.) sublimed (m. p. and mixed m. p. 140°). The melt darkened and became a brownish-black, and, on stronger heating, phthalonitrile distilled up the tube (yield 0·1 g.; m. p. and mixed m. p. 135°). (ii) Di-imino*iso*indoline (0·5 g.) was heated in boiling butanol (25 c.c.) for 100 min., during which ammonia was slowly evolved. The filtrate from traces of blue pigment was evaporated to small bulk and treated with ether (a few drops). Di-imino*iso*indoline (0·1 g.) gradually crystallised having m. p. and mixed m. p. *ca.* 190°. (iii) [With P. F. Clark] Di-imino*iso*indoline (1 g.) was heated in boiling 2-ethoxyethanol (25 c.c.) for 20 hr., during which ammonia was slowly evolved and the solution became greenish and then a faint blue. The filtrate from traces of phthalocyanine was cooled, whereupon tricyanocyaphenine (0·19 g.) separated, having m. p. 300° undepressed by authentic material (Dent and Linstead, *loc. cit.*).

(b) *Formation of phthalocyanine.* (i) Di-imino*iso*indoline (1·8 g.), heated in boiling butanol

(20 c.c.) with succinonitrile (1 g.) for 3·5 hr., evolved ammonia and gave dark needles of phthalocyanine (0·47 g.), and a second crop (80 mg.; total yield, 0·55 g., 34%) after a further hour's boiling; $\lambda_{max.}$ in chloronaphthalene at 6990, 6650, 6400, 6000 Å. (ii) Di-imino*iso*indoline (1 g.), heated in boiling tetralin (25 c.c.) for 100 min., gave beautifully crystalline phthalocyanine (0·4 g., 45%), $\lambda_{max.}$ in chloronaphthalene at 6990, 6640, 6400, 6000 Å. (iii) Only 8 mg. of phthalocyanine ($\lambda_{max.}$ in chloronaphthalene at 6990, 6650, 6000 Å) were obtained by heating the imidine (1 g.) in boiling nitrobenzene (25 c.c.) for 100 min.

(c) *Metal phthalocyanines.* (i) [With MARGARET WHALLEY] Di-imino*iso*indoline (0·2 g.) and nickel chloride (0·2 g.) were dissolved separately in hot formamide (2·5, 12·5 c.c., respectively), and the hot solutions were mixed. Pigment separated almost at once. Next day, the nickel phthalocyanine was collected, washed with ethanol, and extractively crystallised from chloronaphthalene. The yield was 0·19 g., 96%; $\lambda_{max.}$ in chloronaphthalene at 6710, 6030 Å. (ii) The imidine (0·5 g.) and copper powder (0·5 g.) were heated together in boiling butanol (20 c.c.) for 5 min., and the mixture of metal and pigment was collected and washed with methanol. Extractive crystallisation from chloronaphthalene yielded copper phthalocyanine (0·12 g., 24%), $\lambda_{max.}$ in chloronaphthalene at 6780 Å.

Self-condensation of Succinimidine [with JOHN S. FITT].—(a) *Exploratory work.* (i) When succinimidine was heated in boiling ethanol or butanol, alone or with mild dehydrogenating agents ($PhNO_2$, quinones), ammonia was evolved and the solutions became a dark purple, but no tetrazaporphin was formed. (ii) No magnesium tetrazaporphin was obtained by heating succinimidine and magnesium formate or acetate in benzene, toluene, 2-ethoxyethanol, or dibutyl ether, in each case in the presence of quinones, or in 2-ethoxyethanol in the presence of benzoyl peroxide or magnesium oleate, or by heating succinimidine and magnesium acetate in 2-ethoxyethanol with selenium dioxide, hexamethylenetetramine, or nitrobenzene. Heating succinimidine in *cyclo*hexene or dihydronaphthalene with palladium was also ineffective. (iii) Variable small amounts of magnesium tetrazaporphin were formed by short heating of succinimidine with magnesium acetate in nitrobenzene, or with magnesium formate in 2-ethoxyethanol, best in the presence of nitrobenzene.

(b) *Preparation of magnesium tetrazaporphin.* A mixture of succinimidine (1 g.), magnesium formate (10 g.; dried at 75—80°), nitrobenzene (50 c.c.), and 2-ethoxyethanol (50 c.c.; dried over K_2CO_3) was boiled for 15 min., then allowed to cool, and the solid was collected and washed with methanol. The filtrate was evaporated at 100°/20 mm., and the residual nitrobenzene solution run on to a column (14 × 1·5 cm.) of alumina (Spence, type H). The nitrobenzene and a brown impurity were washed through with benzene, and the pigment was eluted with methanol–benzene (1 : 5). The strongly red-fluorescent solution was warmed on the steam-bath until the methanol had distilled out (disappearance of the fluorescence). From the residual benzene, magnesium tetrazaporphin crystallised (average yield, 44 mg., *ca.* 70% pure); $\lambda_{max.}$ in MeOH–C_6H_6 at 5850, 5370 Å. Treatment of the magnesium pigment (69 mg.) with acetic acid (Linstead and Whalley, *J.*, 1952, 4839) gave tetrazaporphin (8 mg.), $\lambda_{max.}$ in C_6H_6 at 6170, 5440 Å.

*Condensation of Succinimidine with Di-imino*iso*indoline: Tribenzotetrazaporphin.*—(a) *Exploratory work.* (i) One equiv. each of succinimidine (2·35 g.) and 1 : 3-di-imino*iso*indoline (3·5 g.) were heated together in boiling *n*-butanol (40 c.c.). Ammonia was evolved, the solution rapidly became dark, and after 2·5 hr. the dark solid (4·1 g.) was collected and washed with ethanol and ether. Continuous extraction of the solid with hot acetone overnight, and then benzene for 3 hr., removed dark brown material and some blue pigment ($\lambda_{max.}$ at 7520, 7210, 6900, 6740, 6530, 5920, 5400 Å). Extraction with hot chlorobenzene for 17 hr. then gave the very dark purplish crude pigment (788 mg.) and a blue supernatant solution, and a charcoal-like residue (2·63 g.) was left in the Soxhlet thimble, from which boiling chloronaphthalene extracted virtually no more pigment. Re-extraction of the crude pigment with hot chlorobenzene overnight gave pigment (662 mg.) which from its absorption spectrum in chlorobenzene appeared to be a mixture (*ca.* 3 : 5) of phthalocyanine and a new pigment with $\lambda_{max.}$ *ca.* 6730, 5920 Å. A substantial separation was achieved by repeated fractional extraction (5 times) with benzene and hot chlorobenzene: the benzene-soluble material and the residues in the Soxhlet thimbles were set aside, whilst the pigment extracted by chlorobenzene was passed to the next extractor (for extraction first with benzene, and then hot chlorobenzene). The crude tribenzotetrazaporphin (113 mg.) crystallised from the chlorobenzene as microscopic dark bluish-purple needles (Found: C, 72·3; H, 3·6; N, 23·9%). Light absorption in chlorobenzene: max. at 6720, 6300, 5920 Å (ε 36,300, 14,500, 37,100). The colour of the solution was peacock-blue. On chromatography of a portion in chlorobenzene on alumina (Spence, type H;

Brockmann grade, II), a green diffuse band washed down the column rapidly, followed slowly by one or two violet-blue bands. The number of blue bands apparently depended on the concentration of the initial solution (they were evidently the result of pigment crystallising out on the column): separate extracts revealed no significant differences. Evaporation of the first green eluate afforded a trace of phthalocyanine, identified spectroscopically ($\lambda_{max.}$ in chloronaphthalene at 7000, 6600, 6400, and 6000 Å). Phthalocyanine is ordinarily insoluble in chlorobenzene: the very dilute solution from the columns was not stable and eventually deposited the pigment. Extraction of the violet-blue bands with hot chlorobenzene gave (with considerable retention on the alumina) a royal-blue solution which fluoresced a weak dull-red in ultraviolet light. The pigment, recovered by evaporation of the solvent, contained 3·9% of ash (Found: C, 70·1; H, 3·5%), which was incompletely removed by aqueous hydrochloric acid (Found: ash, 0·12; C, 71·9; H, 3·7%). Light absorption in chlorobenzene: max. at 6750, 6250, 5920, 3470 Å (ε 61,800, 18,200, 57,600, 53,700). The foregoing benzene extracts were a more reddish-blue, showed a considerably stronger pinkish fluorescence in ultraviolet light, and slightly stronger intensity absorption at *ca.* 6400 Å, which suggested the presence of a further contaminant.

Chromatographic separation of the phthalocyanine from crude pigment mixture was also effected on mucic acid with chlorobenzene. A little phthalocyanine was washed through first, followed slowly by a broad bluish-purple band from which the required pigment was recovered, uncontaminated with ash; and a greenish-blue band, largely of phthalocyanine, formed at the top of the column. The best results were obtained on columns of tartaric acid powder, which neither retained nor destroyed any pigment, and ran rapidly (see below).

(ii) Boiling succinimidine (3 g., 3 equivs.) with 1 : 3-di-imino*iso*indoline (1·5 g., 1 equiv.) in butanol (50 c.c.) for 15 hr. yielded 4 g. of crude charcoal-like product. After exhaustive extraction with methanol and acetone to remove brown material, extraction with benzene and chlorobenzene afforded crude pigment (75 mg.) ($\lambda_{max.}$ in chlorobenzene: 7200, 6750, 6400, 5900, 5480 Å).

(iii) Succinimidine (1 g., 1 equiv.) and 1 : 3-di-imino*iso*indoline (4·3 g., 3 equivs.), heated together in boiling ethanol (40 c.c.) for 15 hr., afforded 1·7 g. of crude product, from which crude pigment (285 mg.) was eventually extracted with benzene and chlorobenzene ($\lambda_{max.}$ in chlorobenzene: 6920, 6740, 6390, 5910, 5460 Å).

(b) *Preparation of crude pigment.* Succinimidine (1 g., 1 equiv.) and 1 : 3-di-imino*iso*indoline (4·3 g., 3 equivs.) were heated together in boiling ethanol (40 c.c.) for 48 hr., and the solid product (4·2 g.) was extracted exhaustively with a hot mixture of methanol (50 c.c.), acetone (50 c.c.), and ethanol (30 c.c.). The crude pigment (3·0 g.) was extracted exhaustively with benzene (yield, 125 mg. of pigment) and then hot chlorobenzene (1·183 g. of pigment). Systematic extraction with these two solvents through 8 stages afforded crude tribenzotetrazaporphin (*a*, 156·5 mg. bulked from benzene extractions; *b*, 419 mg., from chlorobenzene). Both fraction *a* and *b* showed $\lambda_{max.}$ at 5910—5930, 6400—6420, 6740—6770 Å, but the intensity at 6400 Å was higher for *a* than *b*, and *b* showed an additional max. at *ca.* 6920 Å. Chromatography of small samples in chlorobenzene on alumina showed that *a* and *b* were both contaminated by phthalocyanine. Hence the fractions *a* and *b* were combined.

(c) *Chromatographic purification.* The crude tribenzotetrazaporphin (20 mg.) was chromatographed first in chlorobenzene (2 l.) on mucic acid or, better, on powdered tartaric acid hydrate (B.P.; Hopkin and Williams, Ltd.), and the column (6·4 × 30 cm.) was eluted with chlorobenzene. Phthalocyanine was washed through first, followed by the purplish-blue pigment which was recovered (*ca.* 13 mg.) by distillation of the solvent. The pigment (10 mg.) was then chromatographed in benzene (2 l.) on a tartaric acid column (6·4 × 30 cm.) to remove last traces of phthalocyanine, which was again washed through first. Evaporation of the second runnings afforded phthalocyanine-free tribenzotetrazaporphin (recovery, 90%) (Found: C, 71·9; H, 3·75; N, 23·8%). Light absorption in chlorobenzene: max. at 6750, 6400, 5940, 5670, 3480 Å (ε = 72,800, 23,100, 69,700, 24,600, 64,700).

The twice chromatographed pigment (50 mg.) was extracted (Soxhlet) with benzene overnight (yield, 34 mg.) and then chlorobenzene (yield, 16 mg.). The two fractions differed in the intensity of absorption at 6420 Å, the benzene fraction absorbing the more intensely.

The pigment (20 mg.) was finally chromatographed in chlorobenzene (2 l.) on kieselguhr (acid-washed; British Drug Houses, Ltd.) (column, 6·4 × 15 cm.) and eluted with chlorobenzene. A mauve band remained on the column. Evaporation of the eluate and extractive crystallisation of the residue from chlorobenzene gave *tribenzotetrazaporphin* as microscopic very dark bluish needles, decomp. *ca.* 400° (Found: C, 72·2; H, 3·65; N, 24·2. $C_{28}H_{16}N_8$

requires C, 72·4; H, 3·5; N, 24·1%). Light absorption in chlorobenzene: max. at 6750, 5940, 5660, 3490 Å (ε = 78,300, 69,000, 22,900, 59,600); min. at 6500 Å (ε = 12,500) (see Figure).

Oxidation of Tribenzotetrazaporphin with Ceric Sulphate.—Portions of the pigment (13·8, 10·5 mg.) were dusted into separate quantities (5 c.c.) of concentrated sulphuric acid which had been cooled in ice-salt. The solutions were swirled, and each was treated with crushed ice (20 g.) and then 0·00932N-ceric sulphate (10·00 c.c.). The pigment was destroyed almost at once. 0·00760N-Ferrous sulphate (10·00 c.c.) was added to each solution and the excess back-titrated with the ceric sulphate (4·47, 3·00 c.c.), *o*-phenanthroline being used as indicator. The uptake of oxygen was therefore 0·99, 1·00 atom-equiv. (1 mol. of a tetrazaporphin requires 1·0 atom-equiv. of O).

Oxidative Degradation of Tribenzotetrazaporphin.—The pigment (72·8 mg.) was dissolved in concentrated sulphuric acid (2 c.c.; chilled in ice-salt) by stirring. Hydrogen peroxide (*ca.* 1 c.c.; 30-vol.) was added in drops, and the solution removed from the cooling-bath. After 45 min. the solution was light brown. The solution was cooled in ice, and crushed ice (20 g.) was added, followed after 10 min. by powdered ferrous sulphate (1 g.). The solution was extracted with benzene for 22 hr., the extract evaporated, and the residue extracted with dry ether. Evaporation of the latter afforded phthalimide (56·8 mg., 82% of 3 mols.), m. p. and mixed m. p. 230—231°. (There was no loss in weight on treatment with aqueous sodium hydrogen carbonate.) The aqueous solution was then extracted with ether overnight. The extract was evaporated and the residue dried in a vacuum-desiccator ($CaCl_2$). By extraction of the dry residue with dry ether, and evaporation of the latter, a mixture of gum and needles was obtained. Rapid washing with ether removed the gum and left phthalic acid (14·5 mg.), m. p. 190—191° (decomp.).

Oxidative Degradation of Phthalocyanine.—The pigment (74·7 mg.) was oxidised similarly and the solution worked up as above to yield phthalimide (68·0 mg., 79·5% of 4 mols.), m. p. 229—230°, and phthalic acid (unaccompanied by any gum) (17·7 mg.), m. p. 193° (decomp.).

Action of Heat on Tribenzotetrazaporphin.—The pigment was heated in a stream of nitrogen in a " cold-finger " apparatus at 350°/15—20 mm. for 3 hr. A dark blue sticky sublimate was obtained and, higher up the condensing surface, some colourless prisms of phthalonitrile, m. p. and mixed m. p. 141°. Washing the coloured sublimate with cold chlorobenzene gave a green solution (phthalocyanine present) (max. at 5950, 6260, 6740, 6950 Å). The residue on the condensing surface was a hard purplish-blue solid (substantially tribenzotetrazaporphin) (max. in chloronaphthalene at 6750, *ca.* 6250, 5950 Å).

Absorption Spectra.—The instruments used for the light absorption determinations were as described by Linstead and Whalley (*J.*, 1952, 4839). Solutions containing about 0·5 mg. of pigment in 100 c.c. of solvent were used.

Analyses were carried out in the Microanalytical Laboratory (Mr. F. H. Oliver) of this Department.

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1 : 1-*Diethylsulphonyl Derivatives of* L-*Rhamnose and Their Conversion into* 5-*Deoxy*-L-*arabinose.*

By L. Hough and T. J. Taylor.

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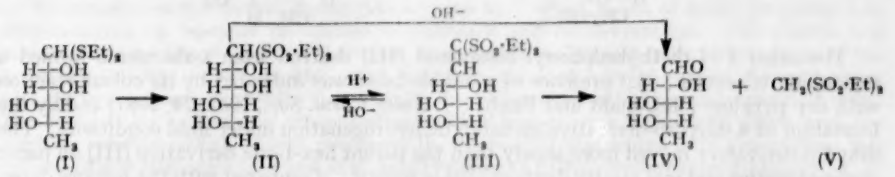
Oxidation of L-rhamnose diethyl dithioacetal (I) with peroxypropionic acid gave a mixture of 1 : 1-diethylsulphonyl-L-*manno*-2 : 3 : 4 : 5-tetrahydroxyhexane (II) and 1 : 1-diethylsulphonyl-L-*arabo*-3 : 4 : 5-trihydroxyhex-1-ene (III). Both were cleaved by dilute aqueous ammonia to give 5-deoxy-L-arabinose (IV) and diethylsulphonylmethane (V).

Aldopentose diethyl dithioacetals are converted into 1 : 1-diethylsulphonyl-3 : 4 : 5-trihydroxypent-1-enes on oxidation with aqueous peroxypropionic acid (Hough and Taylor, *J.*, 1955, 1212), whereas under the same conditions D-mannose diethyl dithioacetal yields

two products, diethylsulphonyl-D-*arabo*pyranosylmethane and 1 : 1-diethylsulphonyl-D-*manno*-2 : 3 : 4 : 5 : 6-pentahydroxyhexane, the latter crystallising from the reaction mixture (McDonald and Fischer, *Biochim. Biophys. Acta.*, 1953, **12**, 203; Hough and Taylor, *Chem. and Ind.*, 1954, 575, 1018). On the other hand, D-galactose and D-glucose diethyl dithioacetals yield only diethylsulphonylpentopyranosylmethanes (Hough and Taylor, *loc. cit.*, p. 1018) which are probably formed from the corresponding hex-1-ene derivatives by ring closure as a result of attack at the cationoid $C_{(2)}$ atom by the terminal primary hydroxyl group. The pent-1-ene derivatives do not cyclise because the carbon chain is not of sufficient length to allow an attack at $C_{(2)}$ (as revealed by molecular models). Thus it was of interest to examine the oxidation of L-rhamnose (6-deoxy-L-mannose) diethyl dithioacetal, since by analogy with D-mannose diethyl dithioacetal it might be expected to yield two acyclic derivatives, a 2 : 3 : 4 : 5-tetrahydroxyhexane (as II) and a 3 : 4 : 5-trihydroxyhex-1-ene (as III), cyclisation of the latter being prevented by the absence of a primary hydroxyl group at $C_{(6)}$.



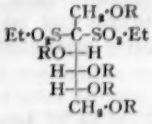
As expected, L-rhamnose diethyl dithioacetal (I) was oxidised by aqueous peroxypropionic acid at room temperature to a mixture of 1 : 1-diethylsulphonyl-L-*manno*-2 : 3 : 4 : 5-tetrahydroxyhexane (II; 49%) and 1 : 1-diethylsulphonyl-L-*arabo*-3 : 4 : 5-trihydroxyhex-1-ene (III; 17%). In the same conditions diethyl dithioacetals of aldoheptoses having the *manno*-configuration also yield acyclic diethylsulphonyl compounds of the saturated type (details to be published). Compounds having this configuration appear to be relatively stable and their isolation is facilitated by their sparing solubility in aqueous solutions. In warm solutions of mineral acid they are converted into the appropriate unsaturated (*e.g.* II ⟶ III) or cyclic derivatives.

The tetrahydroxyhexane (II), which formed a highly crystalline tetra-acetate, was rapidly cleaved by dilute aqueous ammonia to give 5-deoxy-L-arabinose (IV) in good yield and diethylsulphonylmethane (V). Although the classical methods for the descent of the aldose series have been used for the preparation of 5-deoxy-L-arabinose (*e.g.* Fischer, *Ber.*, 1896, **29**, 1381; Ruff and Kohn, *Ber.*, 1902, **35**, 2362; Deulofeu, *J.*, 1930, 2602), the method described herein is undoubtedly more convenient. 5-Deoxy-L-arabinose yielded a highly crystalline benzoylhydrazone. Disproportionation of (II) was also brought about by shaking an aqueous suspension with Amberlite IR-4B (hydroxy-form) resin, but yields of the 5-deoxypentose were low owing to combination of either the sugar or some intermediate with the resin (cf. Hough and Taylor, 1955, *loc. cit.*). Some indication of the instability of the tetrahydroxyhexane (II) in mildly alkaline systems is illustrated by the fact that paper chromatography with a basic solvent caused instantaneous cleavage, and only 5-deoxy-L-arabinose was detected; by using a neutral solvent a streak was obtained owing to degradation during chromatography. The tetrahydroxyhexane (II) could be detected on paper chromatograms when ethyl acetate–acetic acid–water was used as mobile phase. This marked sensitivity of (II) and other saturated acyclic aldose derivatives of this type towards mild base, as compared with the unsaturated derivatives (see later), would also be expected from the diethylsulphonyl derivatives of ketoses (*e.g.* VI; R = H), since they cannot form unsaturated derivatives.

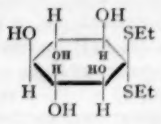
McDonald and Fischer (American Chemical Society Meeting, New York, Sept., 1954) have shown that oxidation of 2 : 2-diethylthio-D-*arabo*-1 : 3 : 4 : 5 : 6-pentahydroxyhexane (D-fructose diethyl dithioacetol) with peroxypropionic acid gave only D-erythrose, none of the intermediate disulphone (VI; R = H) being isolated. However, oxidation of D-*arabo*-1 : 3 : 4 : 5 : 6-penta-*O*-acetyl-2 : 2-diethylthiohexane with peroxyphthalic acid

yielded the corresponding disulphone (VI; R = Ac) which was cleaved with hydrazine to give D-erythrose and diethylsulphonylmethane (McDonald and Fischer, *loc. cit.*) and with methanolic ammonia to give D-erythrose bisacetamide and 1 : 1 : 3 : 3-tetraethylsulphonylpropane [formed by condensation of one molecule of formaldehyde from $C_{(1)}$ of the original hexane derivative with two molecules of diethylsulphonylmethane (Bourne and Stephens, *J.*, **1954**, 4009)]. McDonald and Fischer (*loc. cit.*) have also shown that (VII), the diethyl dithioacetol derived from *myo*inosose-2, could be oxidised by peroxypropionic acid to the corresponding diethylsulphonyl compound, which on treatment with a trace of ammonia disproportionated into *xylo*trihydroxyglutaraldehyde and diethylsulphonylmethane.

(VI)



(VII)



The other 1 : 1-diethylsulphonyl compound (III) derived from L-rhamnose formed a crystalline triacetate; the presence of a double bond was indicated by its colour reaction with dry pyridine (McDonald and Fischer, *J. Amer. Chem. Soc.*, 1952, **74**, 2087) and by the formation of a dihydro-derivative on catalytic hydrogenation under mild conditions. The dihydro-derivative moved more slowly than the parent hex-1-ene derivative (III) on paper chromatograms and was clearly distinguishable from it. Compared with the hexane derivative (II), the hex-1-ene (III) was slowly cleaved by dilute aqueous ammonia (complete in 30 hr.) to give 5-deoxy-L-arabinose (IV), in high yield, and diethylsulphonylmethane. The difference in reaction rate is probably due to a relatively slow addition of the elements of water to the double bond in (III) to give a saturated compound [*e.g.* (II)], which then rapidly disproportionates into the 5-deoxypentose and diethylsulphonylmethane, and the reaction is thus analogous to a reverse aldol condensation (cf. Bourne and Stephens, *loc. cit.*). As in the case of the 1 : 1-diethylsulphonyl-3 : 4 : 5-trihydroxypent-1-enes, the degradation was accompanied by the production of an intense orange-red colour (Hough and Taylor, *loc. cit.*, 1955). This colour reaction was not observed when the tetrahydroxyhexane derivative (II) was cleaved with ammonia, and appears to be characteristic of the αβ-unsaturated disulphones. However, the formation of the colour and of acidic products (Hough and Taylor, *loc. cit.*, 1955) suggests that a side reaction also involving base (cf. colour reaction with pyridine) is operative, since dilute sodium hydroxide solution on (III) causes a similar orange-yellow coloration. It is also noteworthy that aqueous solutions of diethylsulphonyl derivatives of this unsaturated type are weakly acid, whilst those of the saturated acyclic and cyclic types are neutral. Diethylsulphonylmethane is also neutral, but triethylsulphonylmethane is a strong acid (Doering and Levy, *J. Amer. Chem. Soc.*, 1955, **77**, 509).

Oxidation of the tetrahydroxyhexane (II) with sodium metaperiodate at room temperature gave in 2 hr. the expected consumption of 3 mol. of the reagent with subsequent liberation of 3 equiv. of acid, *i.e.*, 2 mol. of formic acid and 1 mol. of diethylsulphonylacetaldehyde. Under the same conditions, the trihydroxyhex-1-ene (III) showed a rapid consumption of 2 mol. of reagent (3 hr.), followed by a slow overoxidation, and thus is analogous to the oxidation of 1 : 1-diethylsulphonyl-D-*threo*-3 : 4 : 5-trihydroxypent-1-ene with sodium metaperiodate (cf. Hough and Taylor, *loc. cit.*, 1955).

Experimental

Evaporations were under reduced pressure. Paper chromatography was performed by the descending method at room temperature on Whatman No. 1 filter paper with butan-1-ol–pyridine–water (10 : 3 : 3 v/v), butan-1-ol–ethanol–water (40 : 11 : 19 v/v), or ethyl acetate–acetic acid–water (9 : 2 : 2 v/v) as mobile phase, ammoniacal silver nitrate being used for the detection of the polyhydroxy-compounds. R_t values are approximate. M. p.s of the disulphones were determined on a Kofler micro-heating stage. Values given for acetyl have been

corrected, to allow for the extra acid that arises in the determination from the sulphone groups. The " acetyl " contents of the parent unacetylated disulphones were determined, and the values adjusted for molecular weight, and then subtracted from those obtained for the corresponding acetylated derivatives.

Peroxypropionic Acid Oxidation of L-*Rhamnose Diethyl Dithioacetal.*—L-Rhamnose diethyl dithioacetal (5·4 g.) in dioxan (15 ml.) was treated with aqueous peroxypropionic acid (150% of theory for 4 mol., based on propionic anhydride; Hough and Taylor, *loc. cit.*, 1955) at room temperature. After 10 min., the mixture was cooled in ice for 1 hr. On concentration of the mixture, needles of 1 : 1-*diethylsulphonyl*-L-manno-2 : 3 : 4 : 5-*tetrahydroxyhexane* (II) (3·3 g.; 49%) separated. Crystallised from ethanol, they had m. p. 178—180°, $[\alpha]_D$ +7·4° (*c*, 4·06 in MeOH) (Found: C, 36·2; H, 6·6. $C_{10}H_{22}O_8S_2$ requires C, 35·9; H, 6·6%). This compound (R_f 0·72) could be detected on paper chromatograms only when the acid solvent was used; under these conditions no deoxypentose was detected. The neutral solvent caused degradation during chromatography and a streak was obtained. With the basic solvent, only 5-deoxy-L-arabinose (R_f 0·56) could be detected.

Evaporation of the mother liquor gave a syrup from which traces of peroxypropionic acid were removed by repeated dissolution in methanol and reconcentration. The residue was dissolved in a minimum quantity of ethanol, the solution cooled, and ether added; more of the derivative (II) (0·4 g.; m. p. 176—178°) was then obtained. On the paper chromatogram, with the basic solvent, it gave the spot (R_f 0·56) due to 5-deoxy-L-arabinose and a trace (R_f 0·81). The syrup (1·5 g.), from the ethanol–ether mother liquors, was boiled with ether, and the resulting solution cooled. Light petroleum (b. p. 40—60°) was added until the solution was opalescent and after some time and at 0°, small rosettes of 1 : 1-*diethylsulphonyl*-L-arabo-3 : 4 : 5-*trihydroxyhex*-1-*ene* (III) (1·1 g.; 17%) were deposited. Recrystallised in a similar manner they had m. p. 105—107°, $[\alpha]_D$ −40·2° (*c*, 4·87 in MeOH), R_f 0·81 (Found: C, 37·8; H, 6·3. $C_{10}H_{22}O_7S_2$ requires C, 38·0; H, 6·3%). A 0·01M-aqueous solution of this compound had pH 3·2 at room temperature.

5-*Deoxy*-L-*arabinose.*—(i) 1 : 1-Diethylsulphonyl-L-*manno*-2 : 3 : 4 : 5-tetrahydroxyhexane (II) (1·13 g.) was dissolved in dilute aqueous ammonia (10 ml.; pH 9—10), and within a few minutes diethylsulphonylmethane (m. p. 101—103°) separated. The mixture, which remained colourless, was kept at room temperature for 16 hr., diethylsulphonylmethane was filtered off, and the filtrate was de-ionised with Amberlite IR-120 and IR-4B resins and then extracted continuously with chloroform for 6 hr. to remove any residual diethylsulphonylmethane. Subsequent concentration gave a pale yellow syrup of 5-deoxy-L-arabinose (0·33 g.; 73%), $[\alpha]_D$ −6·9° (*c*, 2·16 in H_2O). Ruff and Kohn (*loc. cit.*) record $[\alpha]_D$ −5·1°. On paper chromatograms 5-deoxy-L-arabinose gave a yellow spot (R_f 0·56) with the *p*-anisidine hydrochloride spray.

(ii) 1 : 1-Diethylsulphonyl-L-*manno*-2 : 3 : 4 : 5-tetrahydroxyhexane (1 g.) in water (10 ml.) was shaken with Amberlite IR-4B resin (hydroxyl form; 2 g.) for 6 hr. The resin was filtered off and washed by shaking it with water (2 × 50 ml.) for 1—2 hr., and then the combined filtrates were extracted continuously with chloroform for 6 hr. Further washings did not contain 5-deoxy-L-arabinose. Concentration then gave a pale yellow syrup of the 5-deoxypentose (0·09 g.; 22%). More (0·19 g.; 48%) of the chromatographically pure aldose was obtained by shaking the resin with 0·5N-sulphuric acid (150 ml.) for 2 hr., and then with water (2 × 50 ml.) for 1 hr. After neutralisation ($BaCO_3$) and filtration, the liquors were extracted continuously with chloroform for 6 hr. and then evaporated.

(iii) 1 : 1-Diethylsulphonyl-L-*arabo*-3 : 4 : 5-trihydroxyhex-1-ene (122 mg.) was dissolved in dilute aqueous ammonia (5 ml.; pH 9—10), and immediately the solution became yellow and rapidly darkened to orange-red. Paper chromatography indicated that reaction was complete in 30 hr. The 5-deoxypentose (34 mg.; 66%) was isolated as in (i).

The 5-deoxypentose was converted into 5-deoxy-L-*erythro*pentose phenylosazone which had m. p. 172—174° not depressed on admixture with an authentic specimen (Gorin, Hough, and Jones, *J.*, 1953, 2140) [Found by Barry, McCormick, and Mitchell's method (*J.*, 1955, 222): *M*, 317. Calc. for $C_{17}H_{20}O_2N_4$: *M*, 312]. 5-Deoxy-L-arabinose gave a highly crystalline *benzoylhydrazone* when refluxed with benzoylhydrazine (1 mol.) for 1 hr. in a minimum of 98% ethanol. Recrystallisation from 98% ethanol gave small plates, m. p. 192—193° (decomp.) (Found: C, 57·0; H, 6·3. $C_{12}H_{16}O_4N_2$ requires C, 57·1; H, 6·3%).

L-manno-2 : 3 : 4 : 5-*Tetra*-O-*acetyl*-1 : 1-*diethylsulphonylhexane.*—1 : 1-Diethylsulphonyl-L-*manno*-2 : 3 : 4 : 5-tetrahydroxyhexane (0·30 g.) was heated at 95—100° with acetic anhydride (5 ml.) and concentrated sulphuric acid (1 drop) for ½ hr., and the mixture then poured into ice-water. An oil separated which was extracted with chloroform (2 × 50 ml.), and the extract

washed with sodium carbonate solution and then with water and dried ($MgSO_4$). Subsequent concentration gave a pale yellow syrup (0·31 g.; 70%) which crystallised spontaneously. Recrystallised from ether–light petroleum (b. p. 40—60°), the *tetra-acetate* had m. p. 95—98° [Found: C, 43·1; H, 5·9; S, 13·1; Ac, 32·8 (corr.). $C_{16}H_{30}O_{12}S_2$ requires C, 43·0; H, 6·0; S, 12·8; Ac, 34·2%]. The tetrahydroxyhexane (II) gave acid equivalent to 10·6% acetyl.

L-arabo-3 : 4 : 5-*Tri*-O-*acetyl*-1 : 1-*diethylsulphonylhex*-1-*ene*.—1 : 1-Diethylsulphonyl-L-*arabo*-3 : 4 : 5-trihydroxyhex-1-ene (0·21 g.) was acetylated as above, giving a pale yellow syrup (0·23 g.; 81%) which had crystallised after 3—4 weeks. After being dried on a porous tile and carefully washed with benzene–light petroleum, the *triacetate* had m. p 115—116° [Found: C, 43·0; H, 5·7; S, 15·4; Ac, 26·8 (corr.). $C_{16}H_{24}O_{10}S_2$ requires C, 43·3; H, 5·9; S, 14·5; Ac, 29·2%]. The trihydroxyhex-1-ene (III) gave acid equivalent to 15·4% acetyl.

1 : 1-*Diethylsulphonyl*-L-arabo-3 : 4 : 5-*trihydroxyhexane*.—A solution of 1 : 1-diethylsulphonyl-L-*arabo*-3 : 4 : 5-trihydroxyhex-1-ene (III) (0·16 g.) in 95% ethanol (20 ml.) was hydrogenated at 5 atm. for 4—5 hr. in the presence of Raney nickel (2 g.; approx. 3 months old). The pressure and time required for complete reduction of these unsaturated disulphones appear to depend on the age of the Raney nickel [cf. the formation of 1 : 1-diethylsulphonyl-D-*threo*-3 : 4 : 5-trihydroxypentane from the corresponding pent-1-ene (Hough and Taylor, *loc. cit.*, 1955)]. The catalyst was filtered off and the filtrate concentrated. Recrystallisation of the residue from ethanol gave fine *needles* (0·076 g.), m. p. 147°, $[\alpha]_D$ −12·6° (*c*, 0·99 in MeOH), R_f 0·75 (Found: C, 37·9; H, 7·0. $C_{10}H_{22}O_7S_2$ requires C, 37·7; H, 6·9%).

Periodate Oxidation of 1 : 1-*Diethylsulphonyl*-L-manno-2 : 3 : 4 : 5-*tetrahydroxyhexane* (II) *and* 1 : 1-*Diethylsulphonyl*-L-arabo-3 : 4 : 5-*trihydroxyhex*-1-*ene* (III).—(i) *Uptake*. A mixture of *ca.* 0·3M-sodium periodate solution (4 ml.), acetate buffer (pH 3·56; 25 ml.), and disulphone (50—60 mg. accurately weighed) was made up to 100 ml. with water and stored in an amber bottle in the dark. A blank containing none of the disulphone was worked concurrently. At intervals, the periodate uptake was estimated by transferring samples (10 ml.) from the oxidation mixture and the blank, into a mixture of phosphate buffer (pH 7·0; 30 ml.) and 20% potassium iodide solution (5 ml.), then titrating the iodine liberated with 0·01N-sodium thiosulphate solution, starch being used as indicator. This method is superior to that involving titration in acid, in that at pH 7 only the periodate reacts with iodide, and is reduced to iodate. Thus, any iodate which may have reacted during the oxidation is not inadvertently estimated as periodate (cf. Neumüller and Vasseur, *Arkiv. Kemi.*, 1953, **5**, 235).

(ii) *Total acidity*. Solutions of the oxidation mixture and the blank were prepared as above, but the acetate buffer omitted. Acid was determined (Halsall, Hirst, and Jones, *J.*, 1947, 1427) by taking samples (10 ml.) from the oxidation mixture and the blank, adding ethylene glycol (2 ml.) to each, and after a delay of 5 min. to ensure complete destruction of excess of

Time	$NaIO_4$ uptake, mol.		Total acid, equiv.	
hr.	hexane (II)	hex-1-ene (III)	hexane (II)	hex-1-ene (III)
1	2·88	1·26	2·82	1·09
2	2·93	1·73	2·82	1·44
3	2·98	1·98	—	1·67
4	—	2·12	2·82	1·83
6	3·02	2·26	—	1·98
11	—	2·42	—	—
22	—	2·56	—	2·32

periodate, titrating with 0·01N-sodium hydroxide solution, methyl red (screened with methylene blue) being used as indicator. Results are given in the Table.

One of us (T. J. T.) thanks the Department of Scientific and Industrial Research for a Maintenance Grant.

THE UNIVERSITY, BRISTOL. [*Received, May 23rd*, 1955.]

5-*Amino*-9-*phenylphenanthridine*.

By A. E. S. Fairfull, V. Petrow, and (the late) W. F. Short.

[Reprint Order No. 6272.]

By the action of phosphoryl chloride on 2 : 2′-dibenzamidodiphenyl Mamalis and Petrow (*J.*, 1950, 707) obtained a compound, m. p. 164° (hydrochloride, m. p. 335—338°), to which they ascribed the structure 5-amino-9-phenylphenanthridine. Fairfull, Peak, Short, and Watkins (*J.*, 1952, 4703) subsequently obtained 5-amino-9-phenylphenanthridine, m. p. 192—193° (benzoyl derivative, m. p. 214°) from 2-benzamido-2′-phthalimidodiphenyl, *via* 9-phenyl-5-phthalimidophenanthridine. We have now repeated the experiment of Petrow and Mamalis (*loc. cit.*) and find that 2 : 2′-dibenzamidodiphenyl and phosphoryl chloride yield 2-phenyl-4 : 5-6 : 7-dibenzo-1 : 3-diaza*cyclo*hepta-2 : 4 : 6-triene, m. p. 164—165° (isomeric with 5-amino-9-phenylphenanthridine), and 5-benzamido-9-phenylphenanthridine, m. p. 214° (above). The heptatriene has been obtained by Sako (*Mem. Coll. Eng. Kyushu*, 1932, **6**, 263) from 2-amino-2′-benzamidodiphenyl and phosphoryl chloride, and by Fairfull *et al.* (*loc. cit.*, p. 4708) from 2 : 2′-diaminodiphenyl, benzonitrile, and benzenesulphonic acid.

Experimental.—A mixture of 2 : 2′-dibenzamidodiphenyl (3 g.), nitrobenzene (9 c.c.), and phosphoryl chloride (6 c.c.) was boiled under reflux for 2 hr., and the solution was then cooled and repeatedly stirred with warm light petroleum (b. p. 100—120°; 6 × 100 c.c.). The tacky brown solid which separated was dissolved in ethanol (25 c.c.) and mixed with concentrated hydrochloric acid (25 c.c.) and water (15 c.c.). The precipitate solidified directly or after being triturated with ethanol (1—3 c.c.), and the yellow solid (0·6 g.) had m. p. 335—338°. Basification of this hydrochloride and crystallisation from light petroleum (b. p. 100—120°) gave pale yellow prisms of 2-phenyl-4 : 5-6 : 7-dibenzo-1 : 3-diaza*cyclo*hepta-2 : 4 : 6-triene, m. p. and mixed m. p. 164—165°. The acid–ethanol mother-liquor was diluted with water (300 c.c.), filtered through kieselguhr to remove a trace of oil, and then basified to give a white solid, which, recrystallised from toluene, had m. p. 175—185°. The white solid (1·1 g.) from three experiments was heated with ethanol (4 c.c.) and filtered hot from a residue, m. p. 208—211° (0·5 g.). Crystallisation from toluene raised the m. p. to 210—211° (Found: N, 7·6. Calc. for $C_{26}H_{18}ON_2$: N, 7·5%), and the product did not depress the m. p. of 5-benzamido-9-phenylphenanthridine.

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4-*Bromo- and* 4-*Chloro-cholest*-4-*en*-3-*one*.

By J. I. Shaw and Robert Stevenson.

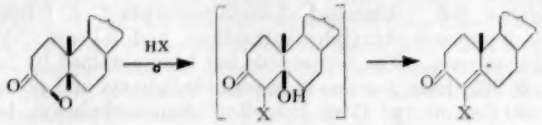
[Reprint Order No. 6346.]

This communication deals with the preparation and ultraviolet light absorption of 4-bromo- (II; X = Br) and 4-chloro-cholest-4-en-3-one (II; X = Cl). Considerable interest has been shown in the effect on the light absorption of halogen substitution on the ethylenic linkage of αβ-unsaturated ketones (Bowden, Braude, and Jones, *J.*, 1946, 948; Bowden and Braude, *J.*, 1952, 1068; Djerassi, Rosenkranz, Romo, Kaufmann, and Pataki, *J. Amer. Chem. Soc.*, 1950, **72**, 4534; Nussbaum, Mancera, Daniels, Rosenkranz, and Djerassi, *ibid.*, 1951, **73**, 3263), and the bathochromic shift observed has made it evident that many structural assignments to unsaturated bromo-ketones in the steroid field were erroneous (see, *e.g.*, Djerassi *et al.*, *loc. cit.*).

The bromo-compound (II; X = Br) was described by Barkow (Diss., Danzig, 1938), and the ultraviolet light absorption, therein reported, was quoted by Dannenberg (*Abhandl. Preuss. Akad. Wiss.*, 1939, **21**, 3) and in subsequent reviews. Because of its equivocal

method of preparation, its unsatisfactory analytical data, and its light absorption ($\lambda_{max.}$ 250 mμ, ε 15,200 in ether), Nussbaum *et al.* (*loc. cit.*) queried the assigned structure and/or purity of this compound, and since the same authors showed that the average bathochromic effect of an α-bromo-substituent in an αβ-unsaturated ketone was 23 mμ, predicted an absorption maximum *ca.* 265 mμ for 4-bromocholest-4-en-3-one (II; X = Br). Application of the standard correction factor for ether (Dannenberg, *loc. cit.*) would give $\lambda_{max.}$ 257 mμ (in EtOH) for Barkow's product.

We have discovered a simple method for the preparation of 4-bromocholest-4-en-3-one. This consists in treatment of 4β : 5-epoxycoprostan-3-one (I) (Plattner, Heusser, and Kulkarni, *Helv. Chim. Acta*, 1948, **31**, 1826) with hydrobromic acid, and involves diaxial opening of the epoxide and spontaneous dehydration of the intermediate β-hydroxy-ketone, to yield the bromide (II; X = Br), $\lambda_{max.}$ 260 mμ (ε 11,500 in EtOH) differing in properties

(I)  (II)

from Barkow's compound. In comparison with the bathochromic shift of +25 mμ observed on substitution of a bromine atom at $C_{(2)}$ in cholest-1-en-3-one (Djerassi and Scholz, *J. Amer. Chem. Soc.*, 1947, **69**, 2404), the bromide (II; X = Br) exhibits a shift of +20 mμ with respect to cholest-4-en-3-one. 4-Chlorocholest-4-en-3-one (II; X = Cl), $\lambda_{max.}$ 256 mμ (ε 11,000 in EtOH), was obtained by brief treatment of the oxide (I) with hydrogen chloride; introduction of an α-chlorine atom into cholest-4-en-3-one causes a shift of +16 mμ, in excellent agreement with the shift (+15 mμ) found for the change cholest-1-en-3-one ⟶ 2-chlorocholest-1-en-3-one (Beereboom and Djerassi, *J. Org. Chem.*, 1954, **19**, 1196; Ellis and Petrow, *J.*, 1953, 3869). Treatment of the bromide (II; X = Br) with zinc in acetic acid gave cholest-4-en-3-one; under the same conditions, the chloride was recovered unchanged.

Unlike the 2α-, 6α-, and 6β-bromo- and -chloro-derivatives of cholest-4-en-3-one, which, when boiled with 2 : 4-dinitrophenylhydrazine in acetic acid, yield cholesta-4 : 6-dien-3-one 2 : 4-dinitrophenylhydrazone (Barton and Miller, *J. Amer. Chem. Soc.*, 1950, **72**, 370, 1066; Djerassi, *ibid.*, 1949, **71**, 1003; Beereboom, Djerassi, Ginsburg, and Fieser, *ibid.*, 1953, **75**, 3500) 4-bromo- and 4-chloro-cholest-4-en-3-one give 2 : 4-dinitrophenylhydrazones with retention of the halogen atom. This parallels the behaviour of 2-bromo- and 2-chlorocholest-1-en-3-one, and provides further examples of the hypsochromic effect (−5 and −6 mμ for the bromo- and the chloro-derivative respectively) of halogen substitution on the ethylenic bond of αβ-unsaturated ketone 2 : 4-dinitrophenylhydrazones.

An attempt to prepare 4-iodocholest-4-en-3-one (II; X = I) by treatment of the oxide (I) with hydriodic acid was unsuccessful, reduction occurring and cholest-4-en-3-one being the sole product isolated.

Experimental.—Rotations were measured in $CHCl_3$ solution at room temperature.

4β : 5-*Epoxycoprostan*-3-*one*. Aqueous 30% hydrogen peroxide solution (20 c.c.) and 4N-sodium hydroxide (20 c.c.) were added simultaneously, dropwise with stirring, to a solution of cholest-4-en-3-one (5·0 g.) in methanol (500 c.c.). After the mixture had been kept at 0° for 48 hr., the solid which had separated was filtered off and crystallised from aqueous methanol, to give 4β : 5-epoxycoprostan-3-one (3·0 g.) as needles, m. p. 118—119°, $[\alpha]_D$ +128° (*c*, 2·5). Plattner *et al.* (*loc. cit.*) give m. p. 116—117°, $[\alpha]_D$ +134°, +136°. The oxide was recovered unchanged after refluxing with periodic acid in aqueous acetone.

4-*Bromocholest*-4-*en*-3-*one*. Aqueous 40% hydrobromic acid (2 c.c.) was added to a solution of the oxide (200 mg.) in chloroform (20 c.c.) and glacial acetic acid (2 c.c.). After 16 hr. at room temperature, the mixture was diluted with water and extracted with chloroform. Removal of the solvent from the washed and dried extract gave an oil which crystallised from aqueous methanol or aqueous acetone to furnish 4-*bromocholest*-4-*en*-3-*one* as long needles (120 mg.), m. p. 114—115°, $[\alpha]_D$ +107° (*c*, 1·4) (Found: C, 70·2; H, 9·7. $C_{27}H_{43}OBr$ requires C, 69·9; H, 9·35%).

Zinc dust (250 mg.) was added portionwise to a solution of the unsaturated bromo-ketone (50 mg.) in acetic acid (30 c.c.) and the mixture refluxed for 4 hr. The product was worked up in the usual way, to give cholest-4-en-3-one, m. p. and mixed m. p. 81—82°. The bromo-ketone was recovered unchanged after treatment under reflux for 1 hr. with collidine.

The bromo-ketone (500 mg.) and 2 : 4-dinitrophenylhydrazine (250 mg.) in acetic acid were heated at 100° for 15 min., and the product was collected and recrystallised from chloroform–ethanol, to yield *4-bromocholest-4-en-3-one 2 : 4-dinitrophenylhydrazone* as red blades, m. p. 217° (decomp.), $\lambda_{max.}$ 262 and 385 mμ (ε 17,000 and 26,800 in $CHCl_3$) (Found : C, 61·9; H, 7·4. $C_{33}H_{47}O_4N_4Br$ requires C, 61·6; H, 7·4%).

4-Chlorocholest-4-en-3-one. A stream of hydrogen chloride was passed through a solution of 4β : 5-epoxycoprostan-3-one (500 mg.) in chloroform (20 c.c.) for 2 min., and the solution then washed with water, dried (Na_2SO_4), and evaporated, to yield an oil which crystallised from aqueous methanol, giving *4-chlorocholest-4-en-3-one* as long needles (450 mg.), m. p. 124·5—125°, $[\alpha]_D$ +106° (*c*, 1·5) (Found : C, 77·65; H, 10·6. $C_{27}H_{43}OCl$ requires C, 77·4; H, 10·3%).

4-Chlorocholest-4-en-3-one 2 : 4-dinitrophenylhydrazone crystallised from ethanol–chloroform as red plates, m. p. 255° (decomp.), $\lambda_{max.}$ 263 and 384 mμ (ε 16,800 and 27,300 in $CHCl_3$) (Found : C, 66·5; H, 7·8. $C_{33}H_{47}O_4N_4Cl$ requires C, 66·2; H, 7·9%). *4-Chlorocholest-4-en-3-one semicarbazone* separated from methanol–chloroform as needles, m. p. 165° (decomp.), $\lambda_{max.}$ 270 mμ (ε 21,000 in EtOH) (Found : C, 70·9; H, 9·3. $C_{28}H_{46}ON_3Cl$ requires C, 70·7; H, 9·7%).

Action of hydriodic acid on 4β : 5-epoxycoprostan-3-one. The epoxy-ketone (500 mg.) was refluxed in freshly distilled 48% hydriodic acid (6 c.c.) and chloroform (25 c.c.) for 1 hr. The solution was washed with water, 10% aqueous sodium thiosulphate, and water, dried (Na_2SO_4), and evaporated. Crystallisation of the residue from methanol gave cholest-4-en-3-one (420 mg.), m. p. and mixed m. p. 81—82°, $[\alpha]_D$ +91° (*c*, 1·4), $\lambda_{max.}$ 240 mμ (ε 17,100 in EtOH).

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THE ROYAL TECHNICAL COLLEGE, GLASGOW. [*Received, April 20th,* 1955.]

O-*Alkylation of Urea.*

By J. W. JANUS.

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IN the direct *O*-methylation of urea with methyl sulphate (Werner, *J.*, 1914, **105**, 927), the isolation of a pure solid derivative from the syrup obtained is difficult and is usually done *via* the picrate (Hughes, Saroff, and Carney, *J. Amer. Chem. Soc.*, 1949, **71**, 2476; Brown and Hoerger, *J. Appl. Chem.*, 1954, **4**, 284). *O*-Methyl*iso*urea hydrochloride has been prepared, however, by addition of methanol to cyanamide in the presence of hydrogen chloride (Stieglitz and McKee, *Ber.*, 1900, **33**, 1517; see also *Org. Synth.*, **34**, 67). It has hitherto been considered necessary to perform the methylation of urea with methyl sulphate at temperatures above 100°, where the reaction may be too violent if large batches are prepared (Werner, *loc. cit.*). It is here shown that urea reacts quietly with methyl sulphate even at room temperature, and the yield is slightly higher. It is, however, no easier to isolate a crystalline derivative from the resulting syrup. For preparative purposes an intermediate temperature is preferred, since the reaction takes some days at room temperature.

It has now been found that urea can also be smoothly methylated with methyl toluene-*p*-sulphonate and the resulting *O*-methyl*iso*urea toluene-*p*-sulphonate can be readily isolated pure and in good yield. The homologue, *O*-ethyl*iso*urea toluene-*p*-sulphonate can be prepared by the analogous reaction.

Experimental.—Methylation with methyl sulphate. Urea (60 g.) and methyl sulphate (126 g.) were stirred together on a water-bath at 40° for 7 hr. Stirring must be such that the urea is completely suspended, for most rapid reaction, and must be continued until after the mixture has become clear. The *iso*urea picrate was precipitated by adding 2M-lithium picrate (350—400 ml.) and alcohol (300 ml.). The mixture was then boiled on the steam-bath for 5 min., the greater part of the picrate dissolving. The mixture was left overnight at 0°, and then

filtered, and the salt washed with ethanol. The air-dried yield was 182 g. (60%), and the m. p. 177°.

The picrate can be converted into the hydrogen sulphate (Hughes *et al.*, *loc. cit.*) or the hydrochloride (Brown *et al.*, *loc. cit.*).

The syrup from the methylation may be used direct for many purposes, but it is advisable to estimate the methyl*iso*urea content by precipitation of the picrate from a small portion (yield 60—64%).

A similar methylation at about 18° required 5 days for completion (3 days to clear). At 60° about 1 hr. is required.

O-*Methylisourea toluene*-p-*sulphonate*. Urea (60 g.) and methyl toluene-*p*-sulphonate (186 g.) were heated together on the steam-bath with mechanical stirring for 3 hr. After ½—1 hr. the temperature rose by 30° and fell again soon after; after 1½ hr. crystals appeared. After the mixture had cooled somewhat, but before complete solidification (50—60°), acetone (200 ml.) was added and the mixture was stirred for 1 hr., left at 0° overnight, and filtered. The O-*methyliso-urea toluene*-p-*sulphonate* was washed with ice-cold acetone (4 × 50 c.c.) and dried (yield 164—167 g., 67%; m. p. 124—126°). Recrystallization may be from acetone (40 ml./g.) or dioxan (15 ml./g.). The compound was discoloured on prolonged boiling with dioxan. Dioxan was heated to 90° and the compound added with vigorous stirring and heating continued for 5 min. The solution was filtered out from 5—12 g. of insoluble matter and an 80% recovery of pure material, m. p. 134°, was obtained on cooling. Recrystallization once from acetone and once from dioxan gives white needles, m. p. 134° (Found: C, 43·7; H, 6·1; N, 11·3; S, 13·1. $C_2H_6ON_2.C_7H_8O_3S$ requires C, 43·9; H, 5·75; N, 11·4; S, 13·05%).

The residue insoluble in hot dioxan was recrystallized from alcohol (6 ml./g.). More than half was recovered as ammonium toluene-*p*-sulphonate. A second recrystallization (10 ml./g.) yielded colourless needles, m. p. 324—326° (decomp.) (Clemo and Walton *J.*, 1928, 726, give 325—330°) (Found: C, 44·15; H, 6·0; N, 7·45. Calc. for $C_7H_{11}O_2NS$: C, 44·4; H, 5·9; N, 7·4%). Analysis (Nessler) of an aqueous solution showed that all the nitrogen was combined as ammonia.

O-*Ethylisourea toluene*-p-*sulphonate*. Urea (6 g.) and ethyl toluene-*p*-sulphonate (20 g.) were heated as above for 7 hr. The waxy solid, obtained on cooling, was dissolved in warm ethyl methyl ketone (50 ml.) and the solution filtered from a small white residue (1·7 g.), m. p. 314—316° (decomp.). The residue was washed with ethyl methyl ketone (5 × 5 ml.), and the filtrate and washings were left in a refrigerator for 3 days with occasional shaking, giving O-*ethylisourea toluene*-p-*sulphonate* (14·75 g.), m. p. 91—93°. Addition of ether to the mother liquors provided a further 1·4 g. (m. p. 90—92°) (total yield 62%). Recrystallization from ethyl methyl ketone (10 ml./g.) at 50—55° removed a further 0·17 g. of insoluble matter and gave a 90% recovery. Recrystallization from ethyl methyl ketone and from *iso*butyl methyl ketone (50 ml./g.) gave m. p. 94° (Found: C, 46·5; H, 6·25; N, 10·65; S, 12·6. $C_{10}H_{16}O_4N_2S$ requires C, 46·15; H, 6·2; N, 10·75; S, 12·3%).

Analyses were by Mr. C. B. Dennis and Miss D. Williams.

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5-*Formyl*-8-*hydroxyquinoline*.

By G. R. CLEMO and R. HOWE.

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IN connection with another problem we have repeated the synthesis (Sen and Ray, *J. Indian Chem. Soc.*, 1932, **9**, 178) of 5- and 7-formyl-8-hydroxyquinoline. Only 5-formyl-8-hydroxyquinoline has now been obtained, as shown by conversion *via* the oxime and nitrile into 8-hydroxyquinoline-5-carboxylic acid (Matsumura and Sone, *J. Amer. Chem. Soc.*, 1931, **53**, 1494). Our aldehyde differs from that reported by Sen and Ray. 5-Formyl-8-hydroxyquinoline has been condensed with dimethylaniline in the presence of hydrochloric acid, and the product obtained was identical with that prepared by Ray (*J. Indian Chem. Soc.*, 1937, **14**, 414) from the alleged 7-formyl-8-hydroxyquinoline. The ultraviolet spectrum of our aldehyde has the characteristics of *p*-hydroxybenzaldehyde and not of salicylaldehyde in accordance with its being the 5-isomer.

Experimental.—Ultraviolet light absorptions were measured in ethanol by using a Hilger Uvispectrometer.

5-Formyl-8-hydroxyquinoline. 8-Hydroxyquinoline (20 g.), ethanol (80 c.c.), and aqueous sodium hydroxide (40 g. in 50 c.c. of water) were refluxed while chloroform (27 g.) was added dropwise during 1 hr. After refluxing for 12 hr., ethanol and excess chloroform were distilled off, the residue was dissolved in water (600 c.c.), and the solution acidified with hydrochloric acid. The solid which separated was dried, and then continuously extracted with light petroleum (b. p. 100—120°). The extract furnished *5-formyl-8-hydroxyquinoline* as straw-coloured needles (2·5 g.), m. p. 173° (from ethanol), giving an emerald colour with aqueous ferric chloride and having $\lambda_{max.}$ 241, 262, and 329 mμ (log ε 4·48, 4·01, 4·03) (Found: C, 69·45; H, 4·1; N, 8·3. $C_{10}H_7O_2N$ requires C, 69·4; H, 4·05; N, 8·1%). The *oxime* formed pale yellow plates, m. p. 196°, from ethanol (Found: C, 63·6; H, 4·4; N, 14·55. $C_{10}H_8O_2N_2$ requires C, 63·8; H, 4·25; N, 14·9%). The *phenylhydrazone* formed brown plates, m. p. 132°, from benzene (Found: C, 72·95; H, 5·3; N, 16·05. $C_{16}H_{13}ON_3$ requires C, 73·0; H, 4·9; N, 16·0%). *8-Acetoxy-5-formylquinoline* gave colourless needles, m. p. 118°, from ethanol (Found: C, 67·2; H, 4·55; N, 6·8. $C_{12}H_9O_3N$ requires C, 67·0; H, 4·2; N, 6·5%).

5-Cyano-8-hydroxyquinoline. Phosphoric oxide (2 g.) was added to the oxime (0·5 g.), dissolved in xylene, and the mixture refluxed for 3 hr. The xylene layer furnished *5-cyano-8-hydroxyquinoline* which formed colourless needles, m. p. 174° (0·2 g.), from light petroleum (Found: C, 70·6; H, 3·95; N, 16·1. $C_{10}H_6ON_2$ requires C, 70·6; H, 3·5; N, 16·5%). The oxime (1 g.), refluxed with acetic anhydride (5 c.c.) for 1 hr., gave *8-acetoxy-5-cyanoquinoline*, colourless needles (0·9 g.), m. p. 150° (from light petroleum) (Found: C, 67·7; H, 3·8; N, 13·0. $C_{12}H_8O_2N_2$ requires C, 67·9; H, 3·8; N, 13·2%). Hydrolysis with aqueous sodium hydroxide gave 5-cyano-8-hydroxyquinoline.

8-Hydroxyquinoline-5-carboxylic acid. 5-Cyano-8-hydroxyquinoline (0·5 g.) was heated on a steam-bath with 80% sulphuric acid (2 c.c.) for 5 hr. The pale yellow needles which separated were collected and washed with water, the filtrate being retained. The needles, after being boiled with water, gave the acid as egg-yellow needles, m. p. and mixed m. p. 272—273° (decomp.) (from ethanol) (cf. Lippmann and Fleissner, *Ber.*, 1886, **19**, 2467), formed a green colour with aqueous ferric chloride, and had $\lambda_{max.}$ 243 and 321 mμ (log ε 4·50 and 3·90) (Found: C, 63·5; H, 3·9; N, 7·3. Calc. for $C_{10}H_7O_3N$: C, 63·5; H, 3·7; N, 7·4%). The hydrochloride separated in colourless columns, m. p. and mixed m. p. 239° (decomp.), from 10% hydrochloric acid (Found: Cl, 16·0. Calc. for $C_{10}H_8O_3NCl$: Cl, 15·7%).

The retained filtrate was neutralised with aqueous ammonia, and the solid collected and washed with water. It was purified by dissolution in dilute aqueous ammonia and reprecipitation with acetic acid. *5-Carbamoyl-8-hydroxyquinoline* was obtained as pale yellow plates, m. p. 264—265° (decomp.), from ethanol (Found: C, 63·8; H, 4·6; N, 14·6. $C_{10}H_8O_2N_2$ requires C, 63·8; H, 4·3; N, 14·9%).

Condensation of 5-formyl-8-hydroxyquinoline with dimethylaniline. The aldehyde (1 g.) and dimethylaniline (2·5 c.c.) were heated on a steam-bath for 30 hr., hydrochloric acid (3 c.c.) being added gradually. The solution was made alkaline and then steam-distilled. The residual blue-green solid was purified by dissolution in hydrochloric acid and reprecipitation with aqueous ammonia, and gave a blue-green powder, m. p. 175—177°, from chloroform–ethanol (Found: N, 10·3. Calc. for $C_{26}H_{27}O_3N$: N, 10·6%). Ray (*loc. cit.*) reports a blue-green powder, m. p. 177° (from chloroform), prepared from the alleged 7-formyl-8-hydroxyquinoline.

2-(8-Hydroxy-5-quinolyl)vinyl phenyl ketone. Acetophenone (2·75 g.) was added with shaking to the aldehyde (4 g.) in warm hydrochloric acid (50 c.c.). The yellow needles which separated on standing were washed with ether, and treatment with aqueous sodium acetate liberated the free *ketone* which forms yellow prisms, m. p. 172° (from ethanol), $\lambda_{max.}$ 249 and 328·5 mμ (log ε 4·52 and 4·32) (Found: C, 78·5; H, 4·8; N, 5·15. $C_{18}H_{13}O_2N$ requires C, 78·55; H, 4·7; N, 5·1%). The *hydrochloride* forms yellow needles, m. p. 247—249° from hydrochloric acid (Found: C, 69·45; H, 4·4; N, 4·6; Cl, 11·65. $C_{18}H_{14}O_2NCl$ requires C, 69·3; H, 4·5; N, 4·5; Cl, 11·4%).

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Paper Chromatography of Uronic Acids.

By R. A. Edington and Elizabeth Percival.

[Reprint Order No. 6400.]

Although paper chromatography of uronic acids has been mentioned in the literature on a number of occasions (Lederer and Lederer, "Chromatography," Elsevier, London, 1953, p. 158—171) there are remarkably few reliable records of the R_G values of the uronic acids and their methyl ethers. This is probably owing, first, to the scarcity of authentic specimens of the uronic acids, and, secondly, to the practical difficulties of "trailing" and poorly defined spots. A number of methylated uronic acids synthesised in this laboratory (Edington, Hirst, and Percival, *J.*, 1955, 2281) were, therefore, examined on the paper chromatogram, various solvent systems and spray reagents being used. Most of the chromatograms were run in a room thermostatically controlled at 21°, although comparable chromatograms run at temperatures between 18° and 21° gave the same R_G values. From preliminary experiments it appeared that for most purposes the two types of solvent system available were, on the one hand, those containing acetic acid, typified by butanol–acetic acid–water, and on the other the butanol–formic acid–water system proposed by Smith *et al.* (*J.*, 1952, 2637). The properties of both of these solvent mixtures slowly change owing to esterification of the acid by the butanol. While Smith and Spriesterbach (*Nature*, 1954, **174**, 467) have recently overcome this difficulty by coating the paper with alginic acid before elution, we have obtained consistent results by the use of an aged or otherwise equilibrated mixture. Although rhamnose has been proposed as a control substance for the paper chromatography of uronic acids, we found that it gave very variable $R_{rhamnose}$ values for the various uronic acids, whereas tetramethylglucose gave reasonably consistent results, the derived R_G values of the uronic acids being generally within 3% of one another on different papers and at different times, butanol–aqueous–formic acid being used. In the case of butanol–acetic acid–water, however, results were less consistent, the maximum variation in the R_G value of the uronic acid being about 6%. The formic acid system has certain other advantages over those containing acetic acid: it is faster, gives better separation, and is much less liable to cause badly shaped spots or trails through incomplete de-ionisation. It is noteworthy that the "heart-shaped spot" which is occasionally mentioned in the literature (Partridge, *Biochem. J.*, 1948, **42**, 238; Reid, *J. Sci. Food Agric.*, 1950, **1**, 234; Chanda, Hirst, and Percival, *J.*, 1951, 1240) as being characteristic of uronic acids has, in the present work, been observed only with solvents containing acetic acid in the presence of inorganic cations. As a rule, the spots are discrete and spherical or elliptical in outline. Aqueous aniline oxalate and butanolic *p*-anisidine hydrochloride were the most generally useful spray reagents. With uronic acids having a free hydroxyl group at $C_{(2)}$, these spray reagents give a brown or reddish-brown colour, whereas with acids substituted at $C_{(2)}$ a brilliant red or purple colour is produced.

Uronic acid	Colour with aniline oxalate	Colour with *p*-anisidine hydrochloride	R_G in BuOH–H·CO_2H–H_2O	R_G in BuOH–AcOH–H_2O
D-Galacturonic acid	Brown	Brown	0·03	0·15
D-Mannuronic acid	Brown	Brown	0·05	0·16
D-Mannuronolactone	Brown	Brown	0·13	0·29
2-*O*-Methyl-D-galacturonic acid	Orange-red	Red-purple	0·20	0·22
D-Glucuronolactone	Brown	Brown	0·21	0·37
4-*O*-Methyl-D-mannuronic acid	Red-brown	Red-brown	0·25	0·29
3 : 4-Di-*O*-methyl-D-galacturonic acid	Red-brown	Red-brown	0·43	0·46
2 : 3-Di-*O*-methyl-D-glucuronic acid	Orange-red	Red-purple	0·47	0·56
2 : 3 : 4-Tri-*O*-methyl-D-galacturonic acid	Orange-red	Red-purple	0·63	0·61
2 : 3 : 4-Tri-*O*-methyl-D-mannuronic acid	Orange-red	Red-purple	0·79	0·80
2 : 3 : 4-Tri-*O*-methyl-D-glucuronic acid	Orange-red	Red-purple	0·84	0·84

Methyl glycosiduronic acids were generally hydrolysed, before chromatography, with N-sulphuric acid at 100° for 24 hr., followed by neutralisation with barium carbonate, filtration, and de-ionisation with Amberlite IR-100-H cation-exchange resin. Butanol–acetic acid–water (40 : 10 : 50) and butanol–formic acid–water (500 : 115 : 385) were either kept at room temperature for 14 days or boiled under reflux for 1 hr. before use.

The Table summarises the results obtained.

CHEMISTRY DEPARTMENT, UNIVERSITY OF EDINBURGH. [*Received, May 7th,* 1955.]

The Infrared Spectra of Some Compounds containing the Pentacyanoferrate Group.

By E. F. G. HERINGTON and W. KYNASTON.

[Reprint Order No. 6412.]

MILLER and WILKINS (*Analyt. Chem.*, 1952, **24**, 1253) have recorded the spectra of solid sodium and potassium ferro- and ferri-cyanide, and Emschwiller (*Compt. rend.*, 1954, **238**, 1414) has reported that the CN group gives rise to a more intense band in the ferro- than in the ferri-cyanides and that these bands appear at wave-numbers 2040 and 2115 cm.$^{-1}$ for the respective potassium salts. The present note records the spectra of the following compounds:

$Na_3[Fe(CN)_5NH_3],6H_2O$; $Na_2[Fe(CN)_5NH_3]H_2O$; $Na_3[Fe(CN)_5H_2O],H_2O$; $Na_2[Fe(CN)_5H_2O]$; $Na_2[Fe(CN)_5NO],2H_2O$ (sodium nitroprusside).

These salts all have sodium as the common cation and contain the group $Fe(CN)_5$ although in some the iron is in the bivalent state and in others in the tervalent state. It has been found that the CN bands occur at the following wave-numbers (cm.$^{-1}$) for the first four of these compounds:

$[Fe^{II}(CN)_5NH_3]^{3-}$	2036,	$[Fe^{III}(CN)_5NH_3]^{2-}$	2126
$[Fe^{II}(CN)_5H_2O]^{3-}$	2043,	$[Fe^{III}(CN)_5H_2O]^{2-}$	2120

The bands in the compounds containing Fe^{II} are broad with half band-widths of about 70 cm.$^{-1}$, while those containing Fe^{III} are narrow with half band-widths of approximately 35 cm.$^{-1}$. Moreover, the intensity of the CN band in these Fe^{II} compounds is approximately twice that in the Fe^{III} compounds; a similar relationship was found for the bands in $[Fe(CN)_6]^{4-}$ and $[Fe(CN)_6]^{3-}$. Thus it appears that the position, shape, and intensity of the CN band in the neighbourhood of 2000 cm.$^{-1}$ are determined by the formal charge on the iron atom and do not depend on the formal charge on the whole anion, since the band appears at the same wave-number in $[Fe^{II}(CN)_5NH_3]^{3-}$ and $[Fe^{II}(CN)_5H_2O]^{3-}$ as in $[Fe^{II}(CN)_6]^{4-}$ and at the same wave-number in $[Fe^{III}(CN)_5NH_3]^{2-}$ and $[Fe^{III}(CN)_5H_2O]^{2-}$ as in $[Fe^{III}(CN)_6]^{3-}$. Alternatively, it may be considered that the CN frequency in $[Fe^{II}(CN)_5X]$ is the same whether X be a neutral group (*e.g.*, NH_3 or H_2O) or a negatively charged ion (*i.e.*, CN^-). A similar relationship exists for the series $[Fe^{III}(CN)_5X]$.

The result for the sodium nitroprusside was unexpected. Formula (I) is the normally accepted structure for the nitroprusside ion (Sidgwick, "Chemical Elements and Their Compounds," Oxford, 1950, p. 1344) although structure (II) is also permissible.

(I) $[(CN)_5Fe{:}N{:::}O{:}]^{2-}$, *i.e.*, $[(CN)_5Fe{-}N{\equiv}O]^{2-}$

(II) $[(CN)_5Fe{::}N{::}\ddot{O}]^{2-}$, *i.e.*, $[(CN)_5Fe{=}N{=}O]^{2-}$

Either structure explains the diamagnetism of the compound. It is known experimentally that the presence of a negative CN group or a neutral NH_3 group or a neutral H_2O

group in the complex $[Fe(CN)_5X]$ (where X = CN, NH_3, or H_2O) has in each case the same effect on the position and intensity of the CN band. Therefore it is reasonable to assume that if the structure of nitroprusside corresponded to formula (I) then the CN band in this compound would probably resemble that in the complexes $[Fe(CN)_6]^{4-}$, $[Fe(CN)_5NH_3]^{3-}$, and $[Fe(CN)_5H_2O]^{3-}$. In fact, the spectrum of the nitroprusside exhibits a narrow band at 2152 cm.$^{-1}$ which is even higher than the frequency of the CN band in the compounds $[Fe(CN)_6]^{3-}$, $[Fe(CN)_5NH_3]^{2-}$, and $[Fe(CN)_5H_2O]^{2-}$ but resembles the band in the latter compounds in shape and intensity. The true nitroprusside structure would appear to be intermediate between that of (I) and (II), *i.e.*, it might be called a resonance mixture. Such an admixture of structures (I) and (II) is likely to have the effect of draining electrons from the Fe atom (to make it resemble Fe^{III} or even Fe^{IV} if formal valency has much meaning) and thus accounts for the high CN frequency.

Moreover, this resonance mixture will give rise to a N–O bond which is intermediate between a double and triple bond and therefore such an admixture of structures (I) and (II) would probably account for the strong band observed at 1938 cm.$^{-1}$ in nitroprusside.*

The spectra of all these compounds in the range 2—15 μ are simple and contain but few bands which are listed in the Table.

Frequencies (cm.$^{-1}$) of main absorption bands.

$Na_3[Fe(CN)_5NH_3]$, $6H_2O$	$Na_2[Fe(CN)_5NH_3]$, H_2O	$Na_2[Fe(CN)_5H_2O]$, H_2O	$Na_2[Fe(CN)_5H_2O]$	$Na_2[Fe(CN)_5NO]$, $2H_2O$
3530 sh.	3550 s.	3390 m.	3400 s.	3580 s.
3360 s.	3360 s.	2043 s.	2152 sh.	3440 sh.
3290 sh.	3290 sh.	1617 m.	2120 s.	2152 s.
2036 s.	2126 s.		2060 w.	1938 s.
1685 sh.	2050 w.		1617 m.	1618 s.
1629 m.	1614 s.			663 m.
1266 m.	1410 w.			
714 w.	1252 s.			
	708 m.			

(s = strong; m = medium; w = weak; sh = shoulder.)

The spectra of the compounds containing co-ordinated H_2O show broad OH bands around 3400 and 1617 cm.$^{-1}$ in addition to the CN bands at 2043 or 2120 cm.$^{-1}$. The compounds containing NH_3 show, in addition to OH bands, extra bands at 3360, 3290, and around 1614—1630 assigned to NH vibrations, together with a fairly strong band in the range 1250—1260 cm.$^{-1}$.

Experimental.—The sample of sodium nitroprusside was used as purchased; specimens of the other salts were prepared according to the directions given by Hofmann (*Annalen*, 1900, **312**, 1). Ground samples of the salts were prepared as pressed KCl discs (Hales and Kynaston, *Analyst*, 1954, **79**, 702), and the spectra were recorded on a double-beam spectrometer (Hales, (*J. Sci. Instr.*, 1953, **30**, 52). The uncertainties in the measurement of the wave-number are believed to be approximately $\pm$10 cm.$^{-1}$ at 2000 cm.$^{-1}$.

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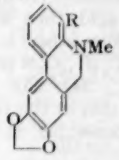
Lycorineanhydromethine.

By T. Shingu, S. Uyeo, and H. Yajima.

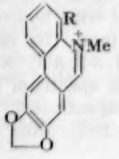
[Reprint Order No. 6433.]

Both lycorineanhydromethine (I) and its dihydro-compound (II) gave crystalline hydriodides which were readily hydrolysed in water. Attempted preparation, however, of their methiodides afforded the corresponding phenanthridinium compounds (III) and (IV), which on treatment with a base yielded as expected the dimeric ethers derived from the pseudo-bases. The phenanthridinium compound (IV) was also prepared by the oxidation of dihydrolycorineanhydromethine (II) with a limited amount of potassium permanganate or with cyanogen bromide; further oxidation of this salt with potassium ferricyanide gave the phenanthridone. Dihydrolycorineanhydromethine was regenerated on treatment of the phenanthridone or the phenanthridinium salt with lithium aluminium hydride.

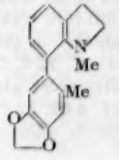
Kondo and Katsura (*Ber.*, 1940, **73**, 1424) claimed to have prepared lycorineanhydromethine methiodide, which they stated had m. p. 226° and on Emde degradation gave lycorineanhydrohydromethine (V). Although we methylated lycorineanhydromethine under conditions similar to those used by the above authors we obtained only the phenanthridinium iodide (III), m. p. 226°, which on Emde degradation did not yield the Emde base (V). We consider it likely that Kondo and Katsura may have made, without recognising it, anhydrolycorine methiodide (VI), m. p. 226° from its corresponding carbonate which we have recently shown (Humber, Kondo, Kotera, Takagi, Takeda, Taylor, Thomas, Tsuda, Tsukamoto, Uyeo, Yajima, and Yanaihara, *J.*, 1954, 4622) accompanies lycorineanhydromethine in the Hofmann degradation of lycorine, and the Emde degradation of the former compound is known (*idem*, *ibid.*) to give the Emde base (V).



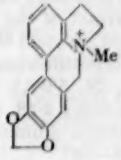
(I; R = $CH{:}CH_2$)
(II; R = Et)



(III; R = $CH{:}CH_2$)
(IV; R = Et)



(V)



(VI)

Experimental.—Ultraviolet spectra were measured for ethanol solutions.

Lycorineanhydromethine hydriodide. The *salt* was prepared by dissolving lycorineanhydromethine in 5% hydriodic acid; it hydrolysed on attempted crystallisation from water but was obtained from ethanol with m. p. 186° (decomp.) (Found: C, 51·9, 52·0; H, 4·2, 4·1. $C_{17}H_{15}O_2N$,HI requires C, 51·9; H, 4·1%).

Dihydrolycorineanhydromethine hydriodide. This *hydriodide* was obtained similarly and had m. p. 210° (from ethanol) (Found: C, 51·3; H, 4·6. $C_{17}H_{17}O_2N$,HI requires C, 51·7; H, 4·6%).

10-*Methyl*-6 : 7-*methylenedioxy*-1-*vinylphenanthridinium iodide* (III). Lycorineanhydromethine (0·3 g.) and methyl iodide (1 ml.) were refluxed for 10 hr. in methanol, then evaporated to dryness. Extraction of the residue with a small quantity of hot water gave, after cooling, the *iodide* (0·12 g.), m. p. 226° (decomp.). For analysis it was dried at 105° for 10 hr. *in vacuo*, the m. p. then being 216° (decomp.) (Found: C, 52·5; H, 3·5. $C_{17}H_{14}O_2NI$ requires C, 52·2; H, 3·6%). The ultraviolet absorption spectrum had $\lambda_{max.}$ 262, 272, 280, and 348 mμ (log ε 4·46, 4·49, 4·51, and 4·10 respectively). The water-insoluble residue from the above extraction yielded unchanged starting material (0·17 g.) from light petroleum.

The iodide (50 mg.) was shaken with lithium aluminium hydride (50 mg.) in absolute ether for 20 min., to afford lycorineanhydromethine (30 mg.), m. p. and mixed m. p. 94—96°. The iodide (III) was dissolved in hot water, aqueous alkali added, and the precipitate taken up in chloroform. Concentration, and recrystallisation of the crystals from ethyl methyl ketone gave the *pseudo-base ether*, m. p. 196° (decomp.) (Found: C, 74·6; H, 5·4. $C_{34}H_{28}O_5N_2$ requires

C, 74·9; H, 5·2%). The product was only slightly soluble in ether, methanol, or ethanol and was converted back into the iodide by hydriodic acid.

1-*Ethyl*-10-*methyl*-6 : 7-*methylenedioxyphenanthridinium iodide* (IV). Dihydrolycorineanhydromethine (0·3 g.) and methyl iodide (2 ml.) in ethanol (6 ml.) were heated in a sealed tube at 100° for 5 hr., then concentrated to dryness. The aqueous extract gave, after chilling and recrystallisation of the product from ethanol, the *iodide* (0·22 g.), m. p. 214°, raised to 236° after drying *in vacuo* at 105° (Found : C, 52·3; H, 4·4. $C_{17}H_{16}O_2NI$ requires C, 52·0; H, 4·1%). The ultraviolet spectrum had $\lambda_{max.}$ 260, 270, 280, and 347 mμ (log ε 4·41, 4·47, 4·48, and 4·01 respectively).

Refluxing dihydrolycorineanhydromethine (0·5 g.) with cyanogen bromide (1·5 g.) in benzene for 6 hr. gave the corresponding *phenanthridinium bromide*, m. p. 228° (decomp.) (from water), which when dried at 100° *in vacuo* or left in the air for a week had m. p. 217° (decomp.) (Found, on a dried sample : C, 57·4, 57·6, 57·4; H, 4·8, 4·9, 4·9; N, 4·0; Br, 22·9. $C_{17}H_{16}O_2NBr,0·5H_2O$ requires C, 57·5; H, 4·7; N, 3·9; Br, 22·5%). This bromide was indistinguishable from that obtained by treatment of the iodide (IV) with silver bromide. Reduction of the bromide with lithium aluminium hydride regenerated dihydrolycorineanhydromethine, m. p. and mixed m. p. 84—86°. Basification of an aqueous solution of the bromide gave the corresponding *pseudo-base ether*, m. p. 213° (decomp.) (from benzene), which after drying had m. p. 218° (decomp.) (Found, on a dried sample : C, 74·4, 74·4; H, 5·8, 5·7; N, 5·6, 5·5. $C_{34}H_{32}O_5N_2$ requires C, 74·4; H, 5·9; N, 5·1%). This compound was only slightly soluble in ether, ethanol, methanol, acetone, or ethyl acetate, but was soluble in chloroform.

0·1% Potassium permanganate solution (11 ml.) was added dropwise to dihydrolycorineanhydromethine (0·2 g.) in acetone (8 ml.), then after 1 hr. the whole was filtered, the filtrate evaporated to dryness, and the residue taken up into chloroform. A hydrochloric acid extract from the chloroform solution, on basification, gave a precipitate, from which ether removed starting material (70 mg.); then crystallisation from benzene yielded the pseudo-base ether (90 mg.), m. p. and mixed m. p. 213° (Found : C, 74·5; H, 5·6; N, 5·3%).

1-*Ethyl*-10-*methyl*-6 : 7-*methylenedioxyphenanthridone*. 1-Ethyl-10-methyl-6 : 7-methylenedioxyphenanthridinium bromide (85 mg.), potassium hydroxide (70 mg.), and potassium ferricyanide (500 mg.) were heated under reflux for 5 hr. in 50% aqueous ethanol (10 ml.). A chloroform extract of the cooled mixture was washed with hydrochloric acid, then water, and concentrated, to yield the *phenanthridone* (53 mg.), m. p. 106° or 114° (from ether) according to the rate of crystallisation (Found : C, 72·5, 72·9; H, 5·5, 5·5; N, 5·2. $C_{17}H_{15}O_3N$ requires C, 72·6; H, 5·4; N, 5·0%). The ultraviolet absorption spectrum had $\lambda_{max.}$ 241, 251, 274, 305, and 340 mμ (log ε 4·58, 4·60, 4·17, 4·03, and 3·65 respectively). Reduction of the phenanthridone with lithium aluminium hydride afforded dihydrolycorine anhydromethine, m. p. and mixed m. p. 85—86°.

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Protection of the Ethynyl Group during Reduction.

By N. A. Dobson and R. A. Raphael.

[Reprint Order No. 6442.]

All the geometrical isomers of undeca-1 : 7-diene-1-carboxylic acid are now known The 1(*cis*) : 7(*cis*)- and the 1(*trans*) : 7(*cis*)-isomer were prepared from the readily available undeca-1 : 7-diyne (Raphael and Sondheimer, *J.*, 1950, 115; 1951, 2693) while the starting materials for the 1(*trans*) : 7(*trans*)- and the 1(*cis*) : 7(*trans*)-isomers were *trans*-1-bromonon-5-ene and *trans*-undec-7-en-1-yne, the preparation of the latter necessitating eight stages from dihydropyran (Crombie, *J.*, 1952, 2997). A procedure is now described for the direct stereospecific conversion of undeca-1 : 7-diyne into *trans*-undec-7-en-1-yne, the 1-ethynyl group of the diyne being protected as the sodium salt by reaction with sodamide in liquid ammonia; reduction of the sodium salt with sodium then reduced only the bilaterally

substituted triple bond with the formation, after hydrolysis, of the *trans*-enyne. At first, preformed sodamide was used but it was later found that sodamide prepared *in situ* from sodium by the usual catalytic procedure was more convenient and gave higher yields. Although the catalyst remained present during the ensuing sodium reduction, it seems that, of the two competing processes, *viz.*, the catalytic conversion of sodium into sodamide and the reduction of a triple bond by sodium, the latter is the more rapid.

A simple, though possibly naïve, explanation of the protective influence of sodium salt formation on an ethynyl group is the consequent development of a negative charge on the terminal carbon atom, a barrier thus being formed against attack by the nucleophilic sodium. The structure of the *trans*-enyne was confirmed by its infrared spectrum and its hydration and hydrogenation to methyl nonyl ketone. The *trans*-enyne was converted into the 1(*trans*) : 7(*trans*)- and the 1(*cis*) : 7(*trans*)-isomer of undecadienecarboxylic acid by the techniques already developed (Raphael and Sondheimer, *loc. cit.*). Thus all four geometrical isomers of the acid can now be made from undeca-1 : 7-diyne.

Experimental.—trans-*Undec-7-en-1-yne.* To a stirred suspension of sodamide (made from sodium, 5·3 g., by the use of ferric nitrate catalyst) in liquid ammonia (450 c.c.) cooled to −40° was added during 30 min. a solution of undeca-1 : 7-diyne (22·2 g.) in ether (23 c.c.), and stirring was continued for a further hour. Sodium (10·5 g.; 50% excess) was then introduced in small pieces during 45 min. Stirring was continued for a further hour and ammonium chloride (9 g.) added. The ammonia was allowed to evaporate overnight through a water-cooled condenser, water and ether were added to the residue, and working up was in the usual fashion. Drying ($MgSO_4$), evaporation, and distillation gave *trans*-undec-7-en-1-yne (17 g., 75%), b. p. 77—78°/19 mm., n_D^{18} 1·4480 (Crombie, *loc. cit.*, gives 82—84°/18 mm., n_D^{20} 1·4462) [Found : C, 87·85; H, 11·9; ·C:CH, 16·0; microhydrogenation (Pd–AcOH) : 3·0 H_2. Calc. for $C_{11}H_{18}$: C, 87·9; H, 12·1; ·C:CH, 16·6%]. The infrared spectrum showed the expected maxima at 970 (C–H deformation associated with *trans*-CH:CH–) and 3300 cm.$^{-1}$ (≡C–H stretching). The *mercury salt* made according to Elsner and Paul's directions (*J.*, 1951, 893) was difficult to purify owing to its extreme solubility in all organic solvents. It was finally obtained as a microcrystalline solid, m. p. 34°, by setting aside a concentrated solution in ethyl acetate (Found : Hg, 41·3. $C_{22}H_{34}Hg$ requires Hg, 40·2%). The *mercury salt* of undeca-1 : 7-diyne crystallised from *n*-propanol in needles, m. p. 38·5° (Found : Hg, 40·5. $C_{22}H_{30}Hg$ requires Hg, 40·5%). A mixture of these two salts liquefied at room temperature.

trans-*Undec-7-en-2-one.* A solution of *trans*-undec-7-en-1-yne (4·4 g.) in ethanol (20 c.c.) was added to a warm mixture of mercuric oxide (1 g.), boron trifluoride–ether complex (0·5 c.c.), trichloroacetic acid (10 mg.), and ethanol (2 c.c.). After 20 hours' shaking at room temperature the mixture was poured into 2N-sulphuric acid, and the product isolated with ether. Drying, evaporation, and distillation gave trans-*undec-7-en-2-one* (3·2 g.), b. p. 100—102°/10 mm., n_D^{16} 1·4491 (Found : C, 78·6; H, 12·0. $C_{11}H_{20}O$ requires C, 78·5; H, 12·0%). The *semicarbazone* crystallised from ethanol in plates, m. p. 99·5—100° (Found : N, 18·9. $C_{12}H_{23}ON_3$ requires N, 18·7%). Catalytic hydrogenation (10% palladium–charcoal in methanol) of the ketone resulted in the uptake of 1 mol. of hydrogen to give methyl nonyl ketone [semicarbazone needles, m. p. 122—123°, from ethanol (Schmalfuss and Treu, *Biochem. Z.*, 1927, **189**, 49, give m. p. 122°)].

Undeca-1(cis) : 7(trans)-*diene*-1-*carboxylic acid.* Treatment of the Grignard derivative of *trans*-undec-7-en-1-yne with carbon dioxide and partial catalytic hydrogenation of the resulting *trans*-undec-7-en-1-yne-1-carboxylic acid according to Crombie's directions (*loc. cit.*) gave undeca-1-(*trans*) : 7(*trans*)-diene-1-carboxylic acid. The physical constants of the two acids and their *S*-benzylthiuronium salts tallied closely with the values reported by Crombie (*loc. cit.*).

trans-1 : 1-*Diethoxydodec-8-en-2-yne.* To a solution of ethylmagnesium bromide [from magnesium (3 g.), ethyl bromide (20 g.), and ether (200 c.c.)] was added one of *trans*-undec-7-en-1-yne (17 g.) in ether (20 c.c.), and the mixture refluxed for 45 min. Ethyl orthoformate (18 g.) in ether (20 c.c.) was run in rapidly, and refluxing continued for a further 6 hr. To the cooled mixture was added ice-cold aqueous acetic acid (50%), and the ethereal layer was washed with sodium hydrogen carbonate solution and water. Drying (Na_2SO_4), evaporation, and distillation gave the *enyne acetal* (19·5 g., 75%), b. p. 112—114°/0·05 mm., n_D^{20} 1·4552 (Found : C, 75·8; H, 11·1. $C_{16}H_{28}O_2$ requires C, 76·15 ; H, 11·2%).

1 : 1-*Diethoxydodeca*-2(cis) : 8(trans)-*diene.* A solution of the above acetal (10·1 g.) in ethyl acetate (100 c.c.) was stirred under hydrogen with 10% palladium–charcoal (1 g.) until 1 mol. of hydrogen had been absorbed (975 c.c. at 21°/752 mm.). Removal of catalyst and solvent

gave the *diene acetal*, b. p. 94—98°/0·1 mm., n_D^{18} 1·4496 (Found: C, 75·5; H, 11·8. $C_{16}H_{30}O_2$ requires C, 75·5; H, 11·9%).

Undeca-1(trans) : 7(trans)-*diene*-1-*carboxylic acid*. A suspension of the preceding diene acetal (5 g.) in water (50 c.c.) and oxalic acid (5 g.) was distilled in steam until no more oil appeared in the condensate. Isolation by means of ether gave *dodeca*-2(trans) : 8(trans)-*dienal*, which, purified by distillation, had b. p. 78—80°/0·04 mm., n_D^{17} 1·4709 (Found: C, 79·3; H, 11·2. $C_{12}H_{20}O$ requires C, 79·9; H, 11·2%). The *semicarbazone* crystallised from ethanol in plates, m. p. 151° (Found: N, 17·6. $C_{13}H_{23}ON_3$ requires N, 17·7%).

The crude aldehyde (2·2 g.) in ethanol (45 c.c.) was mixed with silver nitrate (2 g.) in water (4 c.c.), and N-sodium hydroxide (19 c.c.) was added slowly. After 18 hr. the solid was filtered off and washed with water. Ethanol was removed from the combined filtrates under reduced pressure and the resulting aqueous solution washed with ether. Acidification of the solution with 2N-sulphuric acid and isolation by means of ether gave undeca-1(*trans*) : 7(*trans*)-diene-1-carboxylic acid, b. p. 128—130°/0·1 mm., n_D^{20} 1·4731, crystallising from light petroleum (b. p. 40—60°) in plates, m. p. 35° (Found: C, 73·3; H, 10·3. Calc. for $C_{12}H_{20}O_2$: C, 73·45; H, 10·3%). The *S*-benzylthiuronium salt crystallised from ethyl acetate in plates, m. p. 158—159°. All these properties tally closely with those obtained by Crombie (*loc. cit.*) for the acid prepared by a different route.

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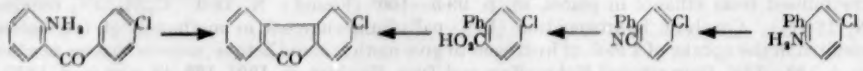
THE QUEEN'S UNIVERSITY, BELFAST. [*Received, May 18th*, 1955.]

The Chlorination of 2-Acetamidofluorene.

By F. BELL and J. A. GIBSON.

[Reprint Order No. 6444.]

ALTHOUGH 2-acetamidofluorene is known to undergo nitration at position 3, the position taken by other entering groups has been assigned only by analogy. In view of the structure of fluorene (Burns and Iball, *Nature*, 1954, **173**, 635) the possibility of substitution in position 1 cannot be excluded. It is now shown that chlorination of 2-acetamidofluorene occurs mainly, or even exclusively, in position 3. The chloro-derivative was oxidised to the chloro-2-acetamidofluorenone, which was hydrolysed and de-aminated to 3-chloro-fluorenone. 3-Chlorofluorenone (I) was prepared (*a*) from 2-amino-4′-chlorobenzophenone (II) and (*b*) from 5-chloro-2-aminodiphenyl (III). The product agreed with that obtained



(II) (I) (III)

by Heilbron, Hey, and Wilkinson (*J.*, 1938, 113) by a Gomberg synthesis. 1-Chloro-fluorenone was prepared for comparison from 1-aminofluorenone, obtained in turn from fluorenone-1-carboxylic acid by the Curtius reaction.

Experimental.—1-*Aminofluorenone*. Fluorenone-1-carboxylic acid (7 g.; prepared from fluoranthene by Fieser's method, *J. Amer. Chem. Soc.*, 1935, **57**, 2174) was converted by thionyl chloride into the acid chloride and this was dissolved in benzene (50 c.c.). Sodium azide (5 g.) was added and the mixture boiled for 8 hr. Sodium hydroxide solution (25 c.c.; 3N) was then added and heating continued for another 2 hr. After evaporation of benzene, the base was extracted with hydrochloric acid, and the extract precipitated with ammonia solution, giving the base (1·1 g.; m. p. 109°) (Goldschmiedt, *Monatsh.*, 1902, **23**, 886, gives m. p. 110° for the base prepared by the Hofmann reaction).

1-*Chlorofluorenone*. 1-Aminofluorenone (1·1 g.) was diazotised in hydrochloric acid, the diazonium solution introduced into cuprous chloride solution, and the mixture distilled in steam.

The resultant **1-*chlorofluorenone*** crystallised from ethanol in yellow, prismatic needles (0·7 g.), m. p. 140° (Found: C, 72·9; H, 3·4. $C_{13}H_7OCl$ requires C, 72·7; H, 3·3%).

2-*Amino*-4′-*chlorobenzophenone*. 2-Toluene-*p*-sulphonamidobenzoic acid (13·6 g.), chlorobenzene (140 c.c.), and phosphorus pentachloride (11 g.) were stirred at 50° for ½ hr. The solution was cooled to 25° and aluminium chloride (27 g.) added; the temperature was then gradually raised to 110° and maintained thereat for 6 hr. After cooling, the mixture was poured on ice, and the chlorobenzene removed in steam. The residue was washed first with dilute hydrochloric acid and then with sodium carbonate solution. The yellowish-brown residue was warmed on a steam-bath for 3 hr. with sulphuric acid (100 c.c.) and then poured on ice and neutralised with ammonia solution. After being kept overnight the product was filtered off and recrystallised from aqueous ethanol. **2-*Amino*-4′-*chlorobenzophenone*** was obtained in bright yellow needles, m. p. 102° (Found: C, 67·4; H, 4·4. $C_{13}H_{10}ONCl$ requires C, 67·4; H, 4·3%).

3-*Chlorofluorenone*. The method was based on that employed by Miller and Bachmann (*J. Amer. Chem. Soc.*, 1935, **57**, 2443) for 3-bromofluorenone. A solution of the diazonium sulphate of 2-amino-4′-chlorobenzophenone was allowed to warm to room temperature and was finally heated on a steam-bath for 20 min. The orange-yellow precipitate was crystallised from ethanol giving 3-chlorofluorenone as yellow platelets, m. p. 159° (Heilbron, Hey, and Wilkinson, *loc. cit.*, give 157°).

2-*Acetamido*-5-*chlorodiphenyl*. Chlorine (1 mol.) was passed into 2-acetamidodiphenyl (13 g.) in chloroform (100 c.c.), the filtered solution was evaporated, and the residue was crystallised from chloroform–light petroleum and then from aqueous ethanol giving material (11·7 g.), m. p. 120—121° (Scarborough and Waters, *J.*, 1927, 93, give 123° as the m. p. of pure 2-acetamido-5-chlorodiphenyl).

2-*Amino*-5-*chlorodiphenyl*. The acetyl derivative (11·5 g.), ethanol (130 c.c.), and concentrated hydrochloric acid (15 c.c.) were boiled for 3 hr. The concentrated solution deposited the hydrochloride, which was filtered off and decomposed with ammonia solution. The resulting oil soon solidified and the solid was recrystallised from methanol. **2-*Amino*-5-*chlorodiphenyl*** formed fawn needles (7·2 g.), m. p. 51° (Found: C, 70·8; H, 4·7. $C_{12}H_{10}NCl$ requires C, 70·8; H, 4·9%).

5-*Chloro*-2-*cyanodiphenyl*. 2-Amino-5-chlorodiphenyl (7 g.) in hydrochloric acid (20 c.c.) and water (20 c.c.) was diazotised, and excess of nitrous acid removed by urea. The cold filtered solution was introduced beneath the surface of a solution containing copper sulphate (13 g.), potassium cyanide (13 g.), and sodium carbonate (10 g.) in water at 25°. The brown, granular precipitate was extracted with ethanol, and the extract precipitated by water. The product, after several recrystallisations from ethanol, formed dark red prisms (3·8 g.), m. p. 100° (Found: C, 73·4; H, 3·9. $C_{13}H_8NCl$ requires C, 73·1; H, 3·7%).

5-*Chlorodiphenyl*-2-*carboxylic acid*. The ***nitrile*** (3·5 g.) in 10% potassium hydroxide–glycol (40 c.c.) was gently boiled for 7 hr. The cooled solution was filtered, diluted with water, and acidified. The product was reprecipitated from ammonia solution and finally recrystallised from aqueous ethanol. 5-Chlorodiphenyl-2-carboxylic acid formed needles (2 g.), m. p. 152° (Found: C, 67·0; H, 3·7. Calc. for $C_{13}H_9O_2Cl$: C, 67·1; H, 3·9%). Cyclisation by sulphuric acid gave 3-chlorofluorenone, m. p. 159° (cf. Heilbron, Hey, and Wilkinson, *loc. cit.*).

Chlorination of **2-*acetamidofluorene*.** Chlorine (1 mol.), considerably diluted by carbon dioxide, was passed into the amide (5 g.) dissolved in cold chloroform (150 c.c.). The precipitate was essentially unchanged material (1·5 g.) but on concentration of the solution material was obtained which, after recrystallisation from acetic acid, gave slightly impure **2-*acetamido*-3-*chlorofluorene*** as fine needles (2·5 g.), m. p. 204° (Found: C, 68·7; H, 4·1. $C_{15}H_{12}ONCl$ requires C, 69·9; H, 4·7%). No further purification was brought about by repeated recrystallisation or use of adsorbents, and the small amount of dichloro-derivative persisted in the following experiments. Hydrolysis by boiling with ethanol–hydrochloric acid gave **2-*amino*-3-*chlorofluorene*,** needles (from aqueous ethanol), m. p. 131° (Found: C, 71·5; H, 4·3. $C_{13}H_{10}NCl$ requires C, 72·4; H, 4·7%). This base was readily deaminated by the ethanol–sulphuric acid–sodium nitrite method to **3-*chlorofluorene*,** which, after distillation in steam and crystallisation from methanol, formed glistening plates, m. p. 95° (Found: Cl, 18·2. $C_{13}H_9Cl$ requires Cl, 17·7%). Sodium dichromate (5 g.) in the minimum of water was added to 2-acetamido-3-chlorofluorene (1 g.) in acetic acid (10 c.c.), and the mixture boiled for 2 hr. The filtered solution on cooling deposited **2-*acetamido*-3-*chlorofluorenone*,** golden-yellow needles (from acetic acid) (0·5 g.), m. p. 260° (Found: C, 66·1; H, 3·8. $C_{15}H_{10}O_2NCl$ requires C, 66·3; H, 3·7%).

2-*Amino*-3-*chlorofluorenone*. A mixture of 2-acetamido-3-chlorofluorenone (1 g.), ethanol

(25 c.c.), amd hydrochloric acid (5 c.c.) was boiled for 2½ hr. and then filtered from the yellow hydrochlorides, which separated on cooling. The bases, liberated by ammonia solution, were dissolved in boiling ethanol. On cooling, purple needles (0·2 g.), m. p. 238—239°, separated; this is probably an impure dichloro-derivative (Found: C, 59·7; H, 2·6. Calc. for $C_{13}H_8ONCl_2$: C, 58·8; H, 3·0%). The filtrate gave red needles (0·3 g.) of *2-amino-3-chlorofluorenone*, m. p. 189° (from ethanol) (Found: C, 68·1; H, 3·6. $C_{13}H_9ONCl$ requires C, 67·7; H, 3·9%). This base was deaminated by the sodium nitrite–ethanol procedure, and the product distilled in steam. The product (m. p. 148—150°) was repeatedly recrystallised from acetic acid, giving 3-chlorofluorenone, m. p. 157—158° (m. p. 158° when mixed with the synthetic sample).

Chlorination of 2-acetamidofluorenone. Chlorine (1 mol.) was passed into 2-acetamidofluorenone (Diels, *Ber.*, 1901, **34**, 1758) in warm acetic acid, and the mixture allowed to cool. The product was 2-acetamido-3-chlorofluorenone (see above).

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HERIOT-WATT COLLEGE, EDINBURGH. [*Received, May 18th*, 1955.]

Reaction of Potassium Bromide–Bromate Solution with Some Sulphur Compounds.

By F. W. SHIPLEY.

[Reprint Order No. 6496.]

ESTIMATION of unsaturation by bromination with potassium bromide–bromate in acid solution has been shown to give reasonably accurate results for many simple alkenes (Francis, *Ind. Eng. Chem.*, 1926, **18**, 821; Mulliken and Wakeman, *Ind. Eng. Chem. Anal.*, 1935, **7**, 59). When, however, the method is applied to certain *cyclo*alkenes and alkadienes (*idem, loc. cit.*; Cortese, *Rec. Trav. chim.*, 1929, **48**, 564) inaccuracies arise which are not substantially reduced by modification of the procedure. Lewis and Bradstreet (*Ind. Eng. Chem. Anal.*, 1940, **12**, 387) report serious inaccuracies introduced by the presence of sulphur compounds.

Application of the method in these laboratories to αβ-unsaturated sulphides, sulphoxides, and related compounds has in many cases led to an unexpectedly high bromine uptake, part of which is associated with scission of the allylic carbon–sulphur bond.

From the compounds studied, the following generalisations appear to hold. (1) Unconjugated carbon–carbon double bonds take up the expected two atoms of bromine. (2) The sulphur atom (in saturated and unsaturated compounds) takes up two atoms (followed by hydrolysis to the sulphoxide; oxidation to the sulphone is negligible). (3) Carbon–sulphur scission does not take place in saturatedc ompounds or in those sulphides in which the allylic carbon atom adjacent to the sulphur atom is primary, but usually occurs when this carbon atom is substituted. (4) Carbon–sulphur scission itself accounts for the uptake of four bromine atoms involving the oxidation of the sulphur-containing moiety to the sulphonic acid, a process analogous to the brominative cleavage of the sulphur–sulphur bond in disulphides reported by Siggia and Edsburg (*Analyt. Chem.*, 1948, **20**, 938). In compounds containing two allylic substituents attached to the sulphur atom, no more than one carbon–sulphur bond is broken. (5) Simple saturated ketones appear to be unattacked. The keto-sulphides examined therefore take up two atoms only (*i.e.* to give sulphoxides).

Exceptions to (3) are methyl 1-methylprop-2-enyl sulphide, where no scission occurs, and 1-dimethylbut-2-enyl phenyl sulphide, where only partial scission appears to take place.

Representative examples are listed in the experimental section. The bromine values quoted are the result of fairly rapid absorption but in certain examples, indicated with an asterisk, further very slow absorption takes place, probably owing to continued scission or substitution.

The absorption of eight atoms of bromine by an alkyl (R′) or aryl (R′)-alkenyl (R) sulphide can be expressed as follows:

$$R(OH)_2Br \xleftarrow{3Br,2H_2O} R\text{—}\overset{|}{\underset{|}{C}}\text{—}S\text{—}R' \xrightarrow{3Br,2H_2O} R'\cdot SO_3H \xrightarrow{2Br,H_2O} R'\cdot SO_3H$$

The unsaturated thio-ester (18) would be expected to follow a similar scheme giving methanesulphonic acid and a substituted *cyclo*pentanecarboxylic acid.

From the bromination of *cyclo*hex-2-enyl phenyl sulphide on a somewhat larger scale, the expected benzenesulphonic acid was identified. From the reaction with ethyl *cyclo*hex-2-enyl sulphide ethanesulphonic acid has not been isolated, but from the non-sulphur fragment, a bromodihydroxy*cyclo*hexane was obtained. That the bromodihydroxy-compound should be produced instead of the expected tribromo-compound strongly suggests the intermediacy of hypobromous acid.

Experimental.—Bromination procedure. The compound to be brominated (0·005—0·01 mole) was dissolved in glacial acetic acid (40 ml.). Water (6 ml.) and concentrated hydrochloric acid (3 ml.) were added and the solution was titrated at room temperature with potassium bromide–bromate solution (0·1N) until a permanent faint yellow coloration was obtained. As a rule, bromine uptake was fairly rapid up to within approximately half an atom of the value shown. The last half atom was usually absorbed rather more slowly, *i.e.*, in a few seconds. Beyond this there was either no uptake or a limited and extremely slow absorption.

	Br absorbed, atoms/mole		Br absorbed, atoms/mole
1. *cyclo*Hexyl methyl sulphide	2	11. *cyclo*Hex-2-enyl methyl sulphide	8
2. *cyclo*Hexyl methyl sulphoxide	0	12. Ethyl *cyclo*hex-2-enyl sulphide	8
3. *cyclo*Hexanone	0 *	13. Di*cyclo*hex-2-enyl sulphide	10
4. 2-Methylthio*cyclo*hexanone	2	14. Di*cyclo*hex-2-enyl ether	4
5. 3-Methylthio*cyclo*hexanone	2	15. *n*-Butyl 1-methylbut-2-enyl sulphide	8
6. *n*-Butyl 2-methylprop-2-enyl sulphide	4 *	16. *cyclo*Hex-2-enyl phenyl sulphide	8
7. *n*-Butyl crotyl sulphide	4	17. *cyclo*Hex-2-enyl methyl sulphoxide	6
8. Diallyl sulphide	6 †	18. Methyl *cyclo*pentene-1-carbothiolate	7·5—8·0
9. Allyl phenyl sulphoxide	2 *	19. *cyclo*Pentene-1-carboxylic acid	2
10. Methyl 1-methylprop-2-enyl sulphoxide	2 *		

† 2 rapidly, 4 in few minutes.

Bromination of cyclo*hex-2-enyl phenyl sulphide.* To the sulphide (0·22 g.) in glacial acetic acid (75 ml.), water (12 ml.), and concentrated hydrochloric acid (6 ml.), there was added, with shaking, the equivalent of eight atoms of bromine as bromide–bromate solution (0·1N). The solution was carefully evaporated to dryness at as little above room temperature as possible and the residue dissolved in hydrochloric acid (4 ml.; 0·5N). After this had been boiled with a solution of *S*-benzylthiuronium chloride (0·2 g.), crystals of *S*-benzylthiuronium benzenesulphonate appeared; these formed plates (from hydrochloric acid), m. p. 148° (literature value 148°) (Found: C, 51·5; H, 5·0; S, 19·7; N, 8·6. Calc. for $C_{14}H_{16}O_3S_2N_2$: C, 51·8; H, 5·0; S, 19·8; N, 8·6%).

The corresponding salt of ethanesulphonic acid could not be isolated (possibly owing to the very high solubility of the latter) from a similar oxidation of ethyl *cyclo*hex-2-enyl sulphide. Part of the oxidation mixture was neutralised (NaOH) and evaporated to dryness, and the residue extracted with chloroform. Removal of the chloroform and distillation [at $100°/10^{-2}$ mm. (bath temp.)] of the residue gave a few drops of somewhat impure bromodihydroxy*cyclo*hexane (Found: C, 37·7; H, 5·7; Br, 40·7. Calc. for $C_6H_{11}O_2Br$: C, 36·9; H, 5·6; Br, 41·0%).

Thanks are expressed to Dr. L. Bateman for valuable advice and to Dr. J. I. Cunneen for helpful criticism and for supplying samples of some of the sulphides. The work forms part of the programme of research of the British Rubber Producers' Research Association.

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Esters Containing Phosphorus. Part XIII. Dialkyl Phosphorobromidates.*

By H. Goldwhite and B. C. Saunders.

[Reprint Order No. 6507.]

Dialkyl phosphorobromidates, $(RO)_2P(:O)\cdot Br$, have been prepared by the action of bromine on trialkyl phosphites (Gerrard and Jeacock, *J.*, 1954, 3647). We have recently found that the reaction between *N*-bromosuccinimide and dialkyl hydrogen phosphites, $(RO)_2P\cdot OH$, proceeds very smoothly, and gives pure phosphorobromidates in good yield (cf. the use of *N*-chlorosuccinimide in the preparation of phosphorochloridates, Kenner, Todd, and Weymouth, *J.*, 1952, 3675). The lower members of the series are liquids which can be distilled under reduced pressure. They are readily hydrolysed, and react instantly with aniline to yield the corresponding *N*-phenylphosphoroamidates, $(RO)_2P(:O)\cdot NHPh$. They also undergo ready thermal decomposition; for example, after 20 min. at 100°, or 72 hr. at 17°, diethyl phosphorobromidate gives a quantitative yield of ethyl bromide, together with a polymeric, bromine-free, residue. The compound can, however, be stored for long periods without change at −40°.

Experimental.—General procedure. To a solution of the dialkyl hydrogen phosphite (0·05 mol.) in dry carbon tetrachloride (20 ml.), *N*-bromosuccinimide (8·9 g., 0·05 mol.) was added in portions (0·5 g.) with shaking and cooling. The solution was cooled to 0° and the succinimide filtered off. Carbon tetrachloride was removed by drawing dry air under reduced pressure through the filtrate at, or a little below, room temperature. The residue was distilled under reduced pressure, with a dry air leak, to yield the pure phosphorobromidate.

Phosphorobromidates, $(RO)_2P(:O)\cdot Br$

			Analysis						
			Found (%)			Reqd. (%)			M. p. and mixed m. p. of *N*-phenylphosphoroamidate [a]
R	Yield	B. p.°/mm.	C	H	Br	C	H	Br	
Me	67	45—47/0·8	13·05	3·2	42·7	12·7	3·2	42·3	88—89° [1]
Et	65	75/1·5	22·0	4·4	37·4	22·1	4·6	36·9	95—96 [2]
Pr^n	45	88—90/0·4	29·3	5·8	32·5	29·4	5·7	32·6	54—55 [3]
Pr^i	65	77—78/0·4	29·9	5·7	32·5	29·4	5·7	32·6	120·5—121 [2]

[a] Authentic samples were prepared by method of: [1] McCombie, Saunders, and Stacey, *J.*, 1945, 921; [2] *Idem*, *J.*, 1945, 380; [3] Ramaswami and Kirch, *J. Amer. Chem. Soc.*, 1953, **75**, 1763.

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OBITUARY NOTICES.

JOHN EDWIN MACKENZIE.

1868—1955.

JOHN EDWIN MACKENZIE, O.B.E., D.Sc., D.Phil.Nat., F.R.S.E., F.H.W.C., Reader (Emeritus) in Chemistry in the University of Edinburgh, died in Edinburgh on February 5th, 1955. He was born on August 31st, 1868, at Helensburgh and received his early education there, under his father, who was headmaster (and owner) of Larchfield Academy. Sir James George Frazer, author of "The Golden Bough," and Alexander Ure, Lord Strathclyde of the Scottish Court of Justice, were former scholars of this Academy. Mackenzie's schooling was completed by a year at the Royal High School, Edinburgh. It would seem that at first he contemplated a career connected with agriculture, for he records that he studied this subject (under Professor Robert Wallace), as well as chemistry and botany. However in 1886 he became a teacher-in-training in London, where his interest in chemistry prompted him to attend the lectures of T. E. Thorpe and F. R. Japp at the Royal College of Science. Returning to Edinburgh next year, he continued his studies at the University and the Heriot-Watt College, and in 1889 graduated as B.Sc. There followed a period of research with W. H. Perkin, junior, and F. S. Kipping, both then on the staff of the Heriot-Watt College, and it was through their influence that chemistry became Mackenzie's main interest. Accordingly, after a spell of teaching at Inverness and Edinburgh, he worked in Fittig's laboratory at Strassburg, obtaining the doctorate (*magna cum laude*) in 1894. He gained the degree of D.Sc. (Edinburgh) in 1901.

During the period 1894—1897 Mackenzie held the post of Assistant Professor of Chemistry at the Heriot-Watt College. In 1897 he was made Head of the Chemistry Department of Birkbeck College. As at this time day classes were added to the usual evening work of the College, Mackenzie had a heavy programme of routine duties, but he contrived to do a considerable amount of research. After eight years at Birkbeck, he accepted the offer of the Principalship of the Victoria Jubilee Technical Institute, Bombay. He resigned this post in 1907 and came back to Edinburgh to hold a Research Fellowship in the Chemistry Department of the University. He was appointed Lecturer in 1908 and held the position of Reader from 1925 until his retirement in 1938.

Mackenzie's researches were mainly in the organic field, but he was also interested in some aspects of inorganic and physical chemistry. Over a period of forty years he published papers, alone or in collaboration, on a variety of topics, including the action of nitric acid on anthracene, the compounds of hydroxides of the alkaline earths with sugars, and the optical rotation of sugars in formamide. Much of his work appeared in the *Transactions* and the *Journal* of the Society; he was a Fellow from 1897 until his death. He was author of a book on the sugars, and joint-author, with Leonard Dobbin, of a textbook of inorganic analysis.

For many years Mackenzie took a keen interest in military training. He served in the Highland Volunteer Artillery at Inverness and in the Bombay Light Horse, and from 1908 to 1922 he was an enthusiastic officer of the Edinburgh Contingent of the O.T.C. As Major in command of the University Battery he was responsible for the training of many young officers during the First World War. His experience of India led to his appointment in 1927 as General Adviser of Indian Students at Edinburgh, and the value of his thirteen years of work in this capacity received fitting recognition when he was made an Officer of the British Empire. Mackenzie was for long a Fellow of the Royal Society of Edinburgh and held office as Member of Council, Curator of the Library, and Secretary to Ordinary Meetings. As representative of the Royal Society of Edinburgh, he served on the Board of Governors of the Heriot-Watt College from 1939 to 1951. Over a long period he was an examiner in chemistry and physics for the Royal College of Veterinary Surgeons.

Mackenzie was an enthusiastic teacher and he was always ready to draw on his long experience for the benefit of colleagues and students. After his retirement he continued to take a lively interest in academic and scientific matters, and during the war he returned to the University to give valuable help in the teaching of first-year students. Owing, no doubt, to his love of games, he retained his physical vigour to a remarkable degree, keeping up his golf until almost the end. His friendliness and sense of humour, his zest in all he did, and his manly character made a lasting impression on all with whom he was associated.

He is survived by his widow and one of his two sons; the other son was killed while on active service during the last war.

T. R. BOLAM.

WILLIAM PUGH.

1897—1955.

WILLIAM PUGH was born at Llannon on January 8th, 1897, the son of a Carmarthenshire farmer, Eleazar Pugh, and his wife Margaret.

Pugh attended the Llanelly County Intermediate School from 1911 to 1915 and then joined the R.A.M.C. as a private, serving in France and Flanders. He was demobilised at the end of 1918, and in January 1919 he entered King's College, London, graduating with First Class Honours in Chemistry in 1921. He came to South Africa in 1922 as lecturer in inorganic chemistry at the University of Cape Town, and in 1938 was appointed Professor and Head of the Department of Chemistry in succession to Professor J. Smeath Thomas. In this capacity he played his full part in University affairs, serving on numerous committees and finally as Dean of the Faculty of Science from 1951 to 1954. He also represented the University on other bodies and in particular on the Board of the Fishing Industry Research Institute.

Before Pugh had had time to settle in to his duties as Head of the Department, the Second World War broke out, and the country's need of technically trained personnel brought a large increase in student numbers, particularly in the elementary classes for students of medicine and engineering. At the same time, graduates left as soon as they obtained their degrees, very few remaining as research students, so that reliable demonstrators were hardly to be found, while only the most vitally urgent additions to the established staff could be considered. All this imposed a heavy load of teaching and administration on the Professor and all his colleagues; nevertheless, Pugh found time to take an active part in the military training of students, being commissioned as lieutenant and then as Acting Captain in the University contingent of the South African Corps of Engineers (Active Citizen Force unit).

The teaching and administrative load continued to be heavy during the post-war years, when the University was called on to undertake the training of a large number of ex-servicemen. Consequently, the formulation of a settled policy of staffing and organization for the Department became possible only after Pugh's return from a period of leave in 1948, and the next year or two were fully occupied in carrying out the initial stages of that policy.

These wartime and post-war difficulties caused a division of Pugh's researches into two main groups, separated by an interval of nearly ten barren years. Shortly before his arrival in Cape Town, the mineral germanite had been discovered at Tsumeb in South West Africa, and soon afterwards Professor Smeath Thomas obtained (through Professor Andrew Young of the Geology Department) a large sample of this material. Pugh's first work was a careful analytical study of this mineral and the devising of methods of extracting germanium and gallium from it, followed by a series of investigations on germanium compounds. The results were published in eleven papers, of which ten appeared in the *Journal*. Later, when one of his research students (Dr. F. Sebba, now a Senior Lecturer at Cape Town) devised an improved method of extracting gallium, Pugh turned his attention to the compounds of that metal, resulting in a further seven papers, six being published in the *Journal*.

Pugh's second fruitful period began towards the end of 1951, soon after he received a copy of Audrieth and Ogg's monograph on "Hydrazine." I went to his room one morning to get his signature to some Departmental papers, and was greeted with "Look at this! I don't believe it!"—he had just read Druce's formula for hydrazinium chlorostannate. Within a very short time he had satisfied himself that Druce was wrong, and from then onwards he and his collaborators have produced a stream of new complex salts of hydrazine and the azines, leading in the end to an excursion into pure organic chemistry (the condensation of carbonyl compounds with salts of secondary amines). Eleven papers have already been published in the *Journal*, and work which he initiated in these fields is still in progress.

Throughout his professional life, however, there was one love to which he constantly returned—analysis. He published seven papers describing new procedures or improvements in existing methods; two of these appeared in the *Journal*, one in the *Analyst*, one in the *J. Appl. Chem.*, and three in the *Trans. Roy. Soc. S. Africa*. At the present time, it is probably his analytical procedures which have brought him widest recognition, though his hydrazine work may well prove to be as important when sufficient time has elapsed for its proper assessment. But it is as a teacher of analysis that he will be most widely remembered in South Africa. It is undoubtedly due to his general attitude to that branch of chemical practice, and to the standards of accuracy which he demanded of his students, that they are to be found in industrial

employment all over Southern Africa. There is thus hardly an industry, from the Cape to the Copper Belt of Northern Rhodesia, where his indirect influence has not been felt in some degree.

The researches of his earlier years gained him the degrees of Ph.D. of Cape Town in 1924, and D.Sc. of London in 1939. He was elected as an Associate of the Royal Institute of Chemistry in 1921, and became a Fellow in 1931, serving as Secretary, as Chairman, and as a member of the committee of the Cape Section. He became a Fellow of the Royal Society of South Africa in 1934 and served on its council. He also served as the first Local Representative of the Chemical Society in South Africa, and in that capacity he attended the Society's Centenary Celebrations in 1947.

In 1924, Pugh married Bessie, daughter of Robert Armour, a Scotsman settled in Cape Town, and had two sons and two daughters. After Mrs. Pugh died in 1938, shortly after the birth of their second daughter, he received much assistance in caring for his children from their aunt, Margaret Armour, whom he subsequently married in 1945.

In July, 1954, Pugh went on leave for the second time, and after a continental tour went to Cambridge for a period of research unhampered by teaching or administrative duties. Soon after he reached Cambridge, he complained of pain, and a medical examination revealed a damaged heart. After a short rest, he seemed to recover, and resumed work in the laboratory, again tackling an analytical problem—the use of ion-exchange columns in the determination of fluoride. Early in March, he wrote that he had found means of overcoming the complications caused by the presence of Group III metals, especially gallium and indium, and immediately afterwards he left for a short holiday in Ireland before writing up his results. He had a severe heart attack on March 11th and died in Dublin on March 12th, 1955. His body was cremated at Pontypridd, near his birthplace, on March 18th, and his ashes were buried at Cape Town, beside the grave of his first wife, on May 13th. He is survived by his widow and children, to one of whom, his elder son, J. R. Pugh, B.Sc., M.B., Ch.B., I am indebted for some of the personal details recorded.

A. H. Spong.

HENRY WREN.

1881—1955.

Henry Wren was born on September 11th, 1881, in London and received his early education at the Wyggeston Grammar School, Leicester. In 1898 he was awarded a major scholarship which he held at Christchurch, Oxford, where he graduated with First Class Honours in chemistry in 1902. Having developed a keen interest in organic chemistry he proceeded to Tübingen University for training in research methods under W. Wislicenus. A joint paper, "Synthesis of Arylnitromethanes and of Stilbene Derivatives" (*Ber.*, 1905, **38**, 502), resulted and Wren was awarded the degree of Ph. D. in 1904.

On his return to England he joined the staff of Birkbeck College, the chemistry department of which shortly afterwards came under the stimulating direction of Alexander McKenzie. Wren entered into McKenzie's programme of stereochemical research with enthusiasm and their joint papers contain experiments now well known to all students of chemistry. They described the asymmetric synthesis of lactic acid by reduction of (−)-bornyl pyruvate (*J.*, 1906, **89**, 688) and the asymmetric synthesis of tartaric acid by oxidation of (−)-bornyl fumarate (*J.*, 1907, **91**, 1215); they prepared many optically active compounds by use of Grignard reagents (*J.*, 1908, **93**, 309) and initiated studies of racemisation phenomena (*J.*, 1909, **95**, 1583) and of the Walden inversion (*J.*, 1910, **97**, 1355).

In 1910 Dr. Wren was appointed Head of the Chemistry Department of the Belfast Technical Institute and there he continued to develop the lines of investigation commenced at Birkbeck College. Over the period 1913—1937 he published in the *Journal* sixteen papers dealing with the stereochemistry and reactions of the diphenylsuccinic acids, the use of borneol and menthol as resolving agents, racemisation phenomena, and Grignard reagents, on which, also, he wrote a short book.

Under his guidance the status of the department continued to rise and the number of students to grow. When Queen's University, Belfast, ceased to be dependent on Dublin it became a matter of urgency to co-ordinate higher education in Northern Ireland. The engineering and chemistry departments of the Technical Institute, by then called the Belfast College of Technology, were recognised as the Faculty of Applied Science and Technology of the new University

and Dr. Wren became the first Professor of Chemistry in this Faculty. Furthermore, his Department became the centre for all advanced instruction in pharmacy in the whole of Northern Ireland. This very considerable expansion in the work of the Chemistry Department occurred without any corresponding increase in the size of the staff and Professor Wren became increasingly occupied with teaching and administrative duties. He still, however, retained a keen interest in the literature of chemistry and with his facility at languages and his flair for picking out immediately all the essentials of a paper he most fortunately became connected with the Bureau of Chemical Abstracts. His name must be very familiar to all who have consulted the Organic Section of British Abstracts and he continued this work until his death.

Professor Wren was a valued member of the local chemical societies in Belfast. Many of the officers and keenest members were his old students and, indeed, his great contribution to chemical education in Northern Ireland and his influence will be felt for many years.

About two years ago Professor Wren left Belfast for the drier climate of Worthing and he died there on February 28th, 1955.

Professor Wren married in 1912 and is survived by his wife, a married daughter and a son, who is a chemist in the Dyestuffs Division of Imperial Chemical Industries Limited.

F. Bell.

PRESIDENTIAL ADDRESS.

DELIVERED AT THE 114TH ANNIVERSARY MEETING OF THE CHEMICAL SOCIETY AT BURLINGTON HOUSE, LONDON, ON MARCH 31ST, 1955.

A Problem in Structural Chemistry.

By W. WARDLAW, C.B.E., D.Sc., F.R.I.C.

THERE is in all well-regulated minds an instinctive love of order. Its appeal is both æsthetic and practical. The mere physical process of arranging, sorting, or classifying a miscellaneous heap of objects gives a certain pleasure. A cupboard of confused odds and ends, a littered desk, arouse in most of us at least an aspiration—not always I fear realised—to put things straight. The pleasure of producing order out of chaos among our possessions—if we really set ourselves to the task—is never-failing. Order is the basis of beauty and harmony as well as efficiency. It is particularly significant in science. A former President of the Chemical Society, Sir Cyril Hinshelwood, has stated in his book, " The Structure of Physical Chemistry " : " Science is not the mere collection of facts, which are infinitely numerous and mostly uninteresting, but the attempt by the human mind to order these facts into satisfying patterns. Now a pattern or design is not a purely objective function but something imposed by the mind on what is presented to it, as is seen in those pictures of piled cubes which can be made at will to appear in advancing or receding order. The imposition of design on Nature is in fact an act of artistic creation on the part of the man of science, though it is subject to a discipline more exacting than that of poetry or painting."

Today I propose to outline an investigation which has given considerable scope for the ordering of facts into satisfying patterns. In doing so I shall keep well in mind the advice of the old proverb which says that the shoemaker should not go beyond his last.

The silicon esters have been known for over a hundred years. The preparation of silicon tetrachloride by Berzelius in 1824 enabled A. Ebelmen in 1846 to produce ethyl and pentyl orthosilicates by the simple reaction, $SiCl_4 + 4ROH = Si(OR)_4 + 4HCl$. Since that time many simple and mixed alkoxides of silicon have been prepared and examined and their physical properties studied and recorded. In marked contrast the corresponding derivatives of titanium and zirconium were obtained for the first time in the twenties of this century. An examination of the boiling points of some of the tetraethoxides of these three elements discloses a remarkable change in physical properties (see Table 1). The important features which emerge from this

TABLE 1.

Alcohol	Boiling point of tetra-alkoxide of: silicon	titanium	zirconium
$CH_3 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot OH$	106·8°/0·5 mm.	155°/1 mm.	253°/0·3 mm.
$CH_3 > CH \cdot CH_2 \cdot OH$	90—91°/0·5 mm.	141°/1 mm.	—
$CH_3 \cdot CH_2 \cdot CH(OH) \cdot CH_3$	86—88°/0·5 mm.	90—92°/0·8 mm.	178°/0·5 mm.
$CH_3 > C \cdot OH$	—	62·3°/1 mm.	46°/0·2 mm.

preliminary survey are : (i) that the increases in boiling points of alkoxides containing a given *n*-alkyl group, when the central atom changes from silcon to titanium to zirconium, are much greater than is expected on the simple basis of increases in molecular weight; and (ii) that the increase in volatility resulting from branching of the alkyl groups, in isomeric alkoxides, is common to the alkoxides of these elements, but the magnitudes of this effect are in the order Zr > Ti > Si.

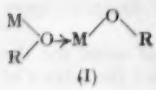
These points suggest that striking differences can be expected in either the degree of molecular complexity or the amount of ionic character in the alkoxides of silicon, titanium, and zirconium. It is also tempting to postulate that increased branching of the alkyl group sterically prevents close intermolecular bonding and thus leads to increased volatility. To test the validity of these ideas the isomeric pentyloxides of silicon, titanium, and zirconium were studied. This series was selected because the molecular weight of the alkyl group remained constant and particularly because little was known about the properties of these compounds. Table 2 summarises the results.

TABLE 2.

Alcohol	Titanium alkoxide			Zirconium alkoxide		
	B. p./mm.	*M*	Mol. comp.	B. p./mm.	*M*	Mol. comp.
$CH_3Me{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}OH$	175°/0·8	565	1·4	256°/0·01	1428	3·2
$CHMe_2{\cdot}CH_2{\cdot}CH_2{\cdot}OH$	148°/0·1	490	1·2	247°/0·1	1462	3·3
$CHMeEt{\cdot}CH_2{\cdot}OH$	154°/0·5	422	1·1	238°/0·1	1615	3·7
$CMe_2{\cdot}CH_2{\cdot}OH$	105°/0·05	500	1·3	188°/0·2	1051	2·4
$CHEt_2{\cdot}OH$	112°/0·05	399	1·0	178°/0·05	868	2·0
$CHMePr^n{\cdot}OH$	135°/1·0	410	1·0	175°/0·05	860	2·0
$CHMePr^i{\cdot}OH$	131°/0·5	415	1·0	156°/0·01	870	2·0
$CMe_2Et{\cdot}OH$	98°/0·1	405	1·0	95°/0·1	455	1·0

In addition it was found that the *n*-pentyloxide of silicon (b. p. 134°/0·1 mm.), although monomeric, was much less volatile than the isomeric *neo*pentyl orthosilicate (b. p. 85°/0·1 mm.). The striking change in volatility of pentyloxides is seen more effectively in Table 2 where the boiling points are compared. The important points which emerge are that branching of the pentyl groups leads to increased volatility in the alkoxides of silicon, titanium, and zirconium but that the effect is most pronounced with the zirconium derivatives. Further it is established that volatility is directly related to molecular complexity (determined ebullioscopically in benzene) in the pentyloxides of zirconium. Although less pronounced, a similar trend in molecular complexity occurs with the titanium derivatives but there is little doubt that all the pentyloxides of silicon are monomeric.

It seems reasonable to suppose that intermolecular bonding accounts for the abnormally high boiling points of the less branched compounds and involves the mechanism (I). This type of molecular association will be strongly opposed when the central atom is shielded by branched alkoxide groups. In the monomeric alkoxides it is evident that the shielding is complete. It may well be that this behaviour is connected with the atomic radius of the central atom. Thus zirconium will require more effective shielding than the smaller silicon or titanium. It is noteworthy that in combination with oxygen the maximum covalency of silicon and titanium is 6 whereas zirconium can exhibit a covalency of 8.



(I)

*neo*Pentylalcohol, although a primary alcohol, has been shown to exhibit a pronounced steric effect in the ordinary reactions of organic chemistry. Both in the case of titanium and of zirconium the boiling points of the tetra*neo*pentyloxides are close to those of their secondary analogues, and their molecular complexity is only slightly higher than that of the secondary alkoxides.

It seems reasonable to suppose that all tetra-*tert.*-alkoxides of titanium and zirconium would be monomeric. This would allow a study to be made of the influence of molecular size on volatility whilst an examination of isomeric higher *tert.*-alkoxides should decide whether structural effects are still important. Further, the influence of the central atom on volatility could be assessed. Accordingly the series of alkoxides $M(O{\cdot}CMe_nEt_{3-n})_4$, $M(O{\cdot}CMe_2R)_4$, and $M(O{\cdot}CMeEtPr^i)_4$ have been prepared and examined where M = Ti or Zr, n = 0, 1, 2, or 3, and R = Me, Et, Pr^n, Pr^i, or Bu^t. In ebullioscopic experiments all the compounds measured were found to be monomeric. Boiling points were measured at several pressures between 0·1 and 10 mm. for the more volatile compounds and in all cases the data fitted straight lines of the form $\log p_{mm.} = a - b/T$ in the pressure range 2—10 mm. The values for the constants a and b are listed in Table 3, together with boiling points (at 5·0 mm. pressure), latent heats of vaporisation (L_v), and entropies of vaporisation at 5·0 mm. ($\Delta S_{5\cdot0}$). The boiling points from Table 3 are plotted against molecular weights in Fig. 1, and the boiling points of the higher alkoxides are given in Table 4. It will be seen that the boiling points do not increase linearly with molecular weight. Moreover the three tertiary heptyloxides gave boiling points in the order

$$M(O{\cdot}CMeEtPr^i)_4 > M(O{\cdot}CEt_3)_4 > M(O{\cdot}CMe_2Bu^t)_4$$

showing clearly that in the monomeric tertiary alkoxides the effect of chain branching is still significant. An interesting point that emerges from Table 3 is that although the latent heats increase with molecular size the entropies of vaporisation are sensibly constant ($42 \pm 2{\cdot}5$ cal. mole^{-1} deg.$^{-1}$) irrespective of whether the central atom is titanium or zirconium, thus emphasising the structural similarity of these compounds. For a given tertiary alkoxide it is seen that there is little difference in the boiling points of the titanium and the zirconium derivative. In fact it appears that the titanium analogue often has the higher boiling point.

Although the results so far considered support the theory that steric effects are most

TABLE 3.

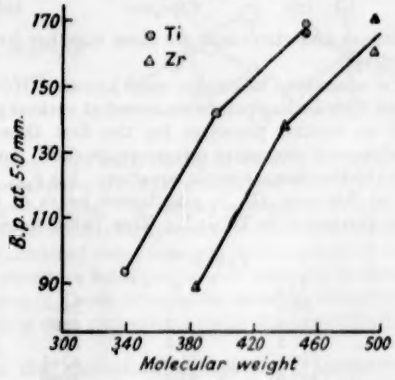
Alkoxide	B. p.	L_v (kcal. mole^{-1})	a	b	$\Delta S_{b.p.}$ (cal. mole^{-1} deg.$^{-1}$)
$Ti(O{\cdot}CMe_3)_4$	93·8°	14·5	9·34	3170	39·5
$Zr(O{\cdot}CMe_3)_4$	89·1	15·2	9·90	3330	42·0
$Ti(O{\cdot}CMe_2Et)_4$	142·7	16·7	9·46	3640	40·0
$Zr(O{\cdot}CMe_2Et)_4$	138·4	16·3	9·34	3550	39·5
$Ti(O{\cdot}CMeEt_2)_4$	170·4	19·0	10·1	4170	43·0
$Zr(O{\cdot}CMeEt_2)_4$	171·4	19·0	10·1	4170	43·0
$Ti(O{\cdot}CMe_2Pr^n)_4$	167·0	19·5	10·4	4270	44·0
$Zr(O{\cdot}CMe_2Pr^n)_4$	161·6	19·0	10·2	2140	44·0

TABLE 4. *Boiling points.*

Alcohol	Ti alkoxide	Zr alkoxide
$CMe_2Pr^i{\cdot}OH$	147°/0·5 mm.	133°/0·1 mm.
$CEt_3{\cdot}OH$	180°/0·5 mm.	180°/0·4 mm.
$CMe_2Bu^t{\cdot}OH$	163°/0·5 mm.	168°/0·5 mm.
$CMeEtPr^i{\cdot}OH$	197°/1·0 mm.	194°/0·7 mm.

important in determining the physical properties of the alkoxides, the alternative explanation that the strong ($+I$) inductive effect of the tertiary alkyl group might be responsible for the striking properties of the tertiary alkoxides must be examined. In an endeavour to resolve

FIG. 1.



these possibilities a detailed study of the following series of secondary alkoxides has been made: $M(O{\cdot}CHR_2)_4$ where R = Me, Et, Pr^n, Pr^i, or Bu^n; and $M(O{\cdot}CHMeR)_4$ where R = Et, Pr^n, Pr^i, Bu^n, Bu^t, or *n*-hexyl. In the first series, the derivatives of the symmetrical dialkylcarbinols, the steric effect will increase rapidly with size of the alkyl group but the $+I$ effect will soon reach saturation. In the other series more gradual steric effects can be achieved. The results are collected in Table 5.

TABLE 5.

	Ti alkoxide			Zr alkoxide		
Alkyl	B. p./0·1 mm.	M	x	B. p./0·1 mm.	M	x
$CHMe_2$	49°	390	1·4	160°	967	3·0
$CHEt_2$	112	399	1·0	181	868	2·0
$CHPr^n_2$	156	500	1·0	163	545	1·0
$CHPr^i_2$	162	474	1·0	158	557	1·0
$CHBu^n_2$	195	—	—	198	—	—
CHMeEt	81	—	—	164	909	2·5
$CHMePr^n$	115	410	1·0	178	860	2·0
$CHMePr^i$	117	415	1·0	176	870	2·0
$CHMeBu^n$	126	—	—	190	—	—
$CHMeBu^t$	127	—	—	128	481	1·0
$CHMe{\cdot}C_6H_{13}$	182	—	—	212	1039	1·7

The contrast between titanium and zirconium is clearly shown. For example, in the dialkylcarbinol series the titanium derivatives, with the exception of the lowest member, are monomeric whereas in the zirconium series the molecular complexity, x, changes from 3 to 2 to 1 as the alkyl

groups are changed from methyl to ethyl to propyl. It is noteworthy that the monomeric secondary alkoxides of zirconium are close in volatility to their titanium analogues as would be expected for monomeric alkoxides. In the alkylmethylcarbinol series the titanium derivatives are monomeric when R in $Ti(O{\cdot}CHMeR)_4$ is propyl or higher, whilst the molecular complexity of the zirconium derivatives decrease from 3 to 2 to 1·7 as the alkyl chain is increased from methyl to ethyl to *n*-hexyl. This behaviour emphasises the steric nature of the effects being investigated since in the zirconium series none of the 1-methylalkoxides shows as complete shielding as the derivatives of the dipropylcarbinols. Moreover the introduction of more remote branching in the alkylmethylcarbinol series considerably enhances the shielding. Thus the zirconium derivative of *n*-butylmethylcarbinol (hexan-2-ol) is complex (*x* between 1·7 and 2·0) and has a much higher boiling point than the monomeric zirconium derivative of the isomeric *tert.*-butylmethylcarbinol (3 : 3-dimethylbutan-2-ol). The evidence so far presented strongly favours the suggestion that it is the steric effect of the alkoxide group and not the $+I$ effect of the alkyl group which is responsible for the remarkable properties of zirconium tetra-alkoxides. This view is supported by the data in Table 6 which show that the boiling points of isomeric

TABLE 6.

Alkyl	$Ti(OR)_4$ B. p./0·1 mm.	$Zr(OR)_4$ B. p./0·1 mm.	Alkyl	$Ti(OR)_4$ B. p./0·1 mm.	$Zr(OR)_4$ B. p./0·1 mm.
$CHMeBu^t$ ...	127°	128°	$CHPr^i_2$	162°	158°
$CMeEt_2$	122	127	CEt_3	166	168
$CHPr^n_2$	156	163	CMe_2Bu^t ...	149	154

monomeric alkoxides of titanium and zirconium are close together irrespective of whether the alkoxide is secondary or tertiary.

Until recently only a few secondary alkoxides were known. However, new silicon tetra-alkoxides have been made and their boiling points measured at various pressures. Boiling points have also been determined at various pressures for the first three members of the series of titanium secondary alkoxides and zirconium tetra*iso*propoxide. In the pressure range 2·0—10·0 mm. the data conformed to the characteristic equation : $\log p_{mm.} = a - b/T$. The values of *a* and *b*, boiling points at 5·0 mm. ($T_{5\cdot0}$), and latent heats of vaporisation at 5·0 mm. ($\Delta S_{5\cdot0}$ cal. mole^{-1} deg.$^{-1}$) are presented in Table 7. This Table shows that although tetra*iso*-

TABLE 7.

Alkoxide	$T_{5\cdot0}$	*a*	*b*	L_v	$\Delta S_{5\cdot0}$
$Si(OPr^i)_4$	55·8°	8·1	2440	11·2	34·0
$Si(O{\cdot}CHEt_2)_4$	139·0	9·7	3690	16·9	40·9
$Ti(OPr^i)_4$	91·3	9·6	3225	14·7	40·5
$Ti(O{\cdot}CHMeEt)_4$	127·8	11·9	4345	19·9	49·6
$Ti(O{\cdot}CHEt_2)_4$	157·3	11·6	4640	21·4	49·6
$Zr(OPr^i)_4$	203·8	15·16	6895	31·5	66·1

propyl and tetra-(1-ethylpropyl) orthosilicate are undoubtedly monomeric they differ by 6·9 units in entropy of vaporisation and that the compound which has the more shielded central atom has unexpectedly the higher entropy of vaporisation. In addition, the monomeric titanium derivative of diethylcarbinol (pentan-3-ol) has an entropy of vaporisation 8·7 units greater than that of its silicon analogue. Hitherto attention has been focused on intermolecular attraction involving oxygen and the central atom in $M(OR)_4$, but these new anomalies suggest that strong intermolecular attraction of another kind, involving the alkyl groups, is also present.

Two mechanisms seem reasonable to explain the abnormally greater degree of structure in the liquid than in the vapour as the size of the alkyl group is increased. The first mechanism involves " entanglement " of neighbouring alkyl groups in the liquid state, thus providing an additional entropy requirement in the vaporisation process, whilst an alternative explanation lies in the possibility that rotation of the alkoxy-groups is more restricted in the liquid than in the vapour. It is clear that alkyl-group interaction would be expected to feature decisively in the properties of the straight-chain normal alkoxides.

The following *n*-alkoxides of titanium and zirconium have been prepared and investigated : $Ti(OC_nH_{2n+1})_4$ where $n = 2$—8 and $Zr(OC_nH_{2n+1})_4$ where $n = 2$—6 or 8. Zirconium tetra-*n*-hexyloxide could not be distilled at 0·05 mm. without decomposition and no attempt was made to distil zirconium tetra-*n*-octyl oxide. Molecular weights (*M*) were determined on freshly distilled alkoxides in boiling benzene and the results, including molecular complexity (*x*) and boiling points, are presented in Table 8. This shows two outstanding features : (*a*) that

TABLE 8.

Alcohol	Titanium alkoxide B. p./0·1 mm.	*M*	*x*	Zirconium alkoxide B. p./0·1 mm.	*M*	*x*
Ethanol	103°	556	2·4	180° *	980	3·6
Propan-1-ol	124	—	—	208	—	—
Butan-1-ol	142	—	—	243	1290	3·4
Pentan-1-ol	158	565	1·4	276	1428	3·2
Hexan-1-ol	176	—	—	300	—	—
Heptan-1-ol	201	—	—	—	—	—
Octan-1-ol	214	781	1·4	—	2046	3·4

* Sublimed.

molecular complexity in the zirconium alkoxides is much greater than in the titanium alkoxides and (*b*) that molecular complexity in both series is little affected by chain length. That molecular complexity is greater in zirconium alkoxides than in the corresponding titanium alkoxides can be explained as due either to stereochemical effects or to a difference in strength of the intermolecular bonding. The stereochemical argument is very strong in view of the greater atomic radius and maximum covalency of zirconium, and evidence is available which suggests that the strength of intermolecular bonding involving titanium and oxygen is comparable with that involving zirconium and oxygen. Caughlan *et al.* (*J. Amer. Chem. Soc.*, 1951, **73**, 5652) have suggested that each titanium atom in the trimeric alkoxides is surrounded octahedrally by oxygen atoms from alkoxide groups and that the trimeric unit comprises three octahedra bound by common faces. A similar arrangement seems reasonable for trimeric zirconium alkoxides but the molecular complexity in zirconium normal alkoxides is significantly greater than three. The fractional value suggests that a species of higher molecular complexity is present, and a possible structure for a pentameric complex is shown in Fig. 2 in which octahedra share edges or faces. These structures involve zirconium with the co-ordination number 6, and the possibility that zirconium attains the co-ordination number 8 in these compounds cannot be ignored.

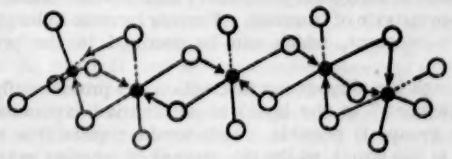


FIG. 2.
R *groups omitted.* $[Zr(OR)_4]_5$.
● = Zr; ○ = *Oxygen.*

It was suggested that the anomalous entropies of vaporisation of certain monomeric alkoxides of silicon and titanium were due to interaction of the alkyl groups, and this conception could be tested by studying the *n*-alkoxides of silicon and titanium. Cullinane *et al.* (*J. Appl. Chem.*, 1951, **1**, 400) gave boiling points at various pressures for the titanium tetra-*n*-alkoxides $Ti(OC_nH_{2n+1})_4$ where $n = 2$—6. Although their data do not conform very accurately to the relation $\log p = a - b/T$, provisional calculations of latent heats and entropies of vaporisation can be made from them. In addition the vapour pressures of tetra-*n*-butyl and tetra-*n*-hexyl orthosilicate have been measured, whilst the data for the tetraethyl orthosilicate have been taken from Post ("Organic Silicon Compounds," Reinhold Publ. Corp., New York, 1949). The latent heats and Trouton constants (Table 9) present strong evidence that alkyl-group interaction occurs in the *n*-alkoxides of silicon and titanium. For tetraethyl orthosilicate the intermolecular attraction involving silicon and oxygen must be relatively small, and it should decrease steadily with increase in size of alkyl group. However, it is found that the entropies of vaporisation increase with alkyl chain length. This effect is partly due to the increase in Trouton's constant with decrease in vapour concentration at 760 mm. at the higher boiling points (cf. Hildebrand, *J. Amer. Chem. Soc.*, 1915, **37**, 970). Accordingly, the entropies of vaporisation

TABLE 9.

Alkoxide	L_v	Trouton const.	Alkoxide	L_v	Trouton const.
$Si(OEt)_4$	11·25	25·7	$Ti(OEt)_4$	21·6	42·5
$Si(OBu^n)_4$	14·84	28·0	$Ti(OPr^n)_4$	15·7	29·1
$Si(O{\cdot}C_6H_{13}{\cdot}n)_4$	21·78	33·5	$Ti(OBu^n)_4$	20·1	35·6
			$Ti(O{\cdot}C_5H_{11}{\cdot}n)_4$	23·1	39·4
			$Ti(O{\cdot}C_6H_{13}{\cdot}n)_4$	24·6	40·5

(cal. deg.$^{-1}$ mole^{-1}), corrected to the same vapour concentration, were calculated and found to be $Si(OEt)_4$ 25·7, $Si(OBu^n)_4$ 27·1, and $Si(O{\cdot}C_6H_{13}\text{-}n)_4$ 31·7. It is suggested that this increase in entropy of vaporisation with increase in chain length is due to molecular "entanglement" in the liquid state. A molecule $(MO{\cdot}C_nH_{2n+1})_4$ can be considered as equivalent to two chains of $(2n + 3)$ atoms fused at the central atom M, and the possibility of entanglement of such tenuous structures is evident. A molecule in the liquid will require special orientation in order to be disentangled before vaporisation, and this increases the entropy of vaporisation. This theory enables one to interpret the surprising order of Trouton constants for the titanium *n*-alkoxides (Table 9). First, the high value for the ethoxide is attributed to the presence of complex molecules involving bonds and it is clear that the vaporisation process in $Ti(OEt)_4$ resembles that of the complex zirconium alkoxides. Thus $\Delta S_{b\cdot p.}$ is 52·6 cal. deg.$^{-1}$ mole^{-1} for $Ti(OEt)_4$ [cf. 59·4 for $Zr(OEt)_4$] and E is 10 kcal. mole^{-1} [cf. 17·6 for $Zr(OEt)_4$]. If allowance is made for the greater shielding of titanium in $Ti(OEt)_4$ (complexity = 2·4) than of zirconium in $Zr(OEt)_4$ (complexity = 3·6) it seems possible that the energy of bonds is approximately the same for M = Ti or Zr. The greater shielding power of propoxide groups explains the decrease in molecular complexity and Trouton constant in passing from the ethoxide to the *n*- or *iso*-propoxide of titanium. Further increase in length of alkyl group leads to an increase in Trouton's constant, which can be ascribed to the predominance of the "entanglement" process.

Although the alkyl-group interaction has provisionally been interpreted as due to molecular "entanglement" in the liquid an alternative explanation in terms of restricted rotation of alkoxide groups is possible. This would require free rotation in the vapour and restricted rotation in the liquid, whilst the amount of rotation in the liquid should decrease with increase in alkyl chain length. Unfortunately, the published data on the dipole moments of these compounds are inconsistent and more accurate measurements are required before a decision can be made.

It has been mentioned that for a given tertiary alkoxide there is little difference in the boiling points of the titanium and the zirconium derivative and it appears that the titanium analogue often has the higher boiling point. From general considerations it would be reasonable to expect that the order of volatilities for the tetra-*tert.*-alkoxides of silicon and the Group IVA elements would be

$$Si(OR)_4 > Ti(OR)_4 > Zr(OR)_4 > Hf(OR)_4 > Th(OR)_4$$

However, it has been established that the order of volatility is Hf > Zr. The boiling points of hafnium alkoxides and analogous zirconium compounds are given in Table 10. It is evident

TABLE 10.

Alkyl	B. p. of $Hf(OR)_4$	B. p. of $Zr(OR)_4$
Ethyl	180—200°/0·1 mm.	180—200°/0·1 mm.
*iso*Propyl	170°/0·35 mm.	172°/0·35 mm.*
tert.-Butyl	90°/6·5 mm.	92·5°/6·0 mm.
tert.-Pentyl	92°/0·1 mm. †	95°/0·1 mm.

* Calc. from 160°/0·1 mm. † Calc. from 106°/0·5 mm.

that the molecular complexity of hafnium alkoxides must be the same as that of the analogous zirconium derivatives. An important feature of this Table is the fact that in no case is a hafnium alkoxide less volatile than its zirconium analogue. As a result of boiling-point measurements in the pressure range 2·0—10·0 mm. on the *tert.*-pentyloxide the latent heat (L_v) and entropy of vaporisation at 5 mm. ($\Delta S_{5\cdot0}$) have been calculated. These results are shown below together with the density ρ (g./c.c.) and molar volume (V_1 c.c.) at 25° :

Alkoxide	$T_{5\cdot0}$	L_v	a	b	$\Delta S_{5\cdot0}$	ρ	V_1
$Zr(O{\cdot}CMe_2Et)_4$	138·4°	16·2	9·34	3550	39·5	0·975	451·1
$Hf(O{\cdot}CMe_2Et)_4$	136·7°	16·3	9·41	3570	39·8	1·159	454·5

It is not surprising to find the close similarity in latent heat, entropy of vaporisation, or molar volume for these two compounds since the chemical similarity of zirconium and hafnium is well established. However the order of volatilities Hf > Zr > Ti demands examination. My colleague, Dr. D. C. Bradley (*Nature*, **1954**, **174**, 323), has directed attention to the fundamental

effect of molecular mass on volatility since it does not support the widely accepted view that volatility decreases with rising molecular weight. The latter view relies on the various empirical relations between molecular weight and boiling point but it has no theoretical basis. By contrast the fundamental effect of mass on volatility has a theoretical background and affords a rational explanation of certain boiling-point anomalies. Bradley points out that the fundamental effect is clearly revealed by the comparison of vapour pressures of compounds differing only in isotopic composition (isotopic molecules). These comparisons are least complicated by differences in intermolecular forces and it can be assumed that differences in vapour pressures are due to the effect of mass alone. The relative vapour pressures of isotopic molecules vary in a complex manner and it is intriguing to find that the lighter species is not always the more volatile. In fact the review by Clusius (*Z. Elektrochem.*, 1938, **44**, 21) of hydrogen and deuterium compounds shows that the relative vapour pressures vary with temperature in the sense that higher temperatures favour the volatility of the heavier species. Similar behaviour by other isotope molecules was reported by Urey (*J.*, 1947, 576) and by Stokland (*Kgl. Norske Videnskab. Selskab*, 1939, **12**, 122, 126). However, this peculiar behaviour is explicable in terms of statistical thermodynamics, although a rigorous treatment seems to be confined to simple cases such as that given by Ubbelohde (" Modern Thermodynamics," Oxford, 1952, p. 169). Bradley contends that if this mass effect is fundamental then it should be a general phenomenon recognisable whenever vapour pressures of two compounds are compared. However, it is a second-order effect usually obscured by the greater effect caused by differences in intermolecular forces and is only apparent under certain conditions such as obtain in the case of isotopic molecules. This theory predicts a super-isotope effect as a general phenomenon occurring in centrosymmetric systems such as $M'X_n$ and $M''X_n$ where M′ and M″ are *n*-valent elements with nearly identical atomic radii and X is a univalent shielding group. Besides zirconium and hafnium, it seems likely that the compounds of niobium and tantalum and also molybdenum and tungsten might fulfil these conditions. A survey of the literature revealed that this is indeed the case as is shown in Table 11, which gives data for pairs of compounds in which the heavier species is

TABLE 11.

	NbF_5	TaF_5	$NbCl_5$	$TaCl_5$	MoF_6	WF_6
Formula weight	187·9	275·9	270·2	358·2	210·0	297·9
Boiling point	234·9°	229·2°	254·0°	239·3°	35·0°	17·5°
Radius of orbital atom (Å)	1·34	1·34	1·34	1·34	1·36	1·37
Molar heat of vaporization (kcal. $mole^{-1}$)	12·9	13·0	13·2	13·6	8·34	8·69

the more volatile. The relative boiling points of these " anomalous " pairs are quite inexplicable in terms of the conventional empirical rule connecting volatility and molecular weight, yet this behaviour is expected on the basis of what is here proposed as the fundamental effect of molecular weight on volatility.

In view of the conclusions arrived at to explain the remarkable physicochemical properties of the alkoxides of titanium, zirconium, and hafnium it is of interest to extend the investigation to tertiary alkoxides of thorium also. Eight new alkoxides $Th(OR)_4$ have been prepared by alcohol interchange involving thorium tetra*iso*propoxide and the appropriate alcohol :

$$Th(OPr^i)_4 + 4ROH \longrightarrow Th(OR)_4 + 4Pr^iOH$$

Molecular weights were determined ebullioscopically in benzene and, where possible, boiling points were measured under reduced pressure. The data, including the calculated molecular complexities ($x = M$/formula weight), are recorded in Table 12.

TABLE 12. *Thorium tetra-alkoxides.*

Alkyl	B. p./mm.	*M*	*x*	Alkyl	B. p./mm.	*M*	*x*
CMe_3	160°/0·1 (subl.)	1787	3·4	CMe_2Pr^i		1444	2·3
CMe_2Et	208°/0·3	1601	2·8	CEt_3	148°/0·05	714	1·0
$CMeEt_2$	148°/0·1	1156	1·8	$CMeEtPr^n$	153°/0·1	1171	1·7
CMe_2Pr^n	Decomp. 120°/0·1	1653	2·6	$CMeEtPr^i$	139°/0·05	709	1·0

The thorium derivative of ethylmethyl*iso*propylcarbinol (2 : 3-dimethylpentan-3-ol) appears to be the most volatile organic compound of thorium yet recorded and several of the other compounds listed in Table 12 are more volatile than the thorium–tetra(acetylacetone) complex, the only other volatilisable organic thorium compound hitherto reported.

It is evident from Table 12 that the volatility and molecular complexity of thorium alkoxides are determined by the size and shape of the alkyl group. There can be little doubt that this

behaviour is predominantly the result of stereochemical effects. Thus there will be only minor variations in electronic effect from one alkyl group to another because they are all tertiary alkyl. Moreover, the molecular complexities decrease with increase in size of the alkyl group and this behaviour is consistent with the stereochemical theory previously advanced to account for the behaviour of the alkoxides of silicon, titanium, zirconium, and hafnium. This theory suggests that intermolecular bonding M···O involving the central atom M (= Ti, Zr, or Hf) and oxygen from a neighbouring alkoxide group gives rise to complex non-volatile alkoxides. In the monomeric alkoxides the central atom is shielded by the rotation of the branched alkoxide groups, intermolecular attraction is minimised, and the compounds are relatively volatile. The theory was supported by a comparison of the behaviour of the alkoxides of silicon, titanium, zirconium, and hafnium. This showed that the size of the central atom controlled the effectiveness of an alkoxide group in shielding. Thus the effect of chain branching on volatility was much greater for zirconium (or hafnium) than for titanium, and least for silicon. Thorium, whose atomic radius is the largest of those of the Group IVA elements, gives alkoxides with properties which accord with these stereochemical requirements. The contrast in the properties of thorium, zirconium, titanium, and silicon alkoxides is demonstrated in Table 13, which contains the boiling points (0·1 mm.) and molecular complexities (in parentheses) of selected compounds having an increasing degree of chain branching of the alkyl group.

TABLE 13.

	Si	Ti	Zr	Th
Atomic radius (Å)	1·17	1·36	1·48	1·65
Alkoxyl				
O·CH_2Me	−15° * (1·0)	102° (2·4)	180° (3·4)	Non-volatile
O·$CHMe_2$	15 (1·0)	49 (1·4)	160 (3·0)	210° (3·8)
O·CMe_3	—	52 (1·0)	50 (1·0)	160 (3·4)
O·$CMeEt_2$	—	128 (1·0)	128 (1·0)	148 (1·8)
O·CEt_3	—	166 (1·0)	166 (1·0)	154 (1·0)

* Calculated.

An interesting feature of Table 13 is the behaviour of the monomeric tertiary C_7-alkoxides of titanium, zirconium, and thorium. Their boiling points are close together, suggesting that they have similar molar heats of vaporisation because the effect of the central atom has been obviated by the screen of organic groups. This emphasises the powerful effect of highly branched alkoxide groups in shielding a central atom. Thus, in addition to suppressing the intermolecular attraction involving the central atom and oxygen, it appears that the contribution due to the marked ionic character in the thorium alkoxide is also nullified.

I have confined my remarks to investigations involving quadrivalent elements. It will be recognised, however, that my subject today is capable of wide extension and already striking results have been obtained from a study of the alkoxides of the quinquevalent elements, niobium and tantalum, and sexavalent uranium.

It seems possible that these volatile derivatives of the metals may have important industrial applications where high purity is required. Preliminary experiments show that distilled zirconium alkoxides are spectroscopically pure with respect to many common metallic impurites. Moreover, it is possible to separate hafnium from zirconium by high-efficiency fractional distillation. A new method for the separation of niobium and tantalum by means of their alkoxides is also foreshadowed. The ability to prepare the alkoxides in a high state of purity and the ease with which they can be converted into the pure oxide is of great value, particularly when the metal can be derived by reduction of the oxide.

The investigator in any field of investigation must realise that however convincing his conclusions may seem they may require correction and modification when brought into relation with wider considerations. There is always the danger that the specialist, having formed opinions for himself, develops a parental affection for them which becomes emotional rather than scientific. On the other hand, accurate experimental data are incontestable and the attempt of the human mind to order facts into patterns is very satisfying.

From the earliest times the practitioners of a particular art have always shown a tendency to draw apart from the rest of the community and to constitute themselves a separate class or fraternity. The conception of a learned society such as the Chemical Society is different. It exercises, not a narrow and sectional influence, but an influence both broad and catholic which traverses national frontiers and which, by promoting free trade in all beneficent discoveries, advances the welfare of humanity at large.

ONE HUNDRED AND FOURTEENTH ANNUAL GENERAL MEETING.

THE One Hundred and Fourteenth Annual General Meeting of the Chemical Society was held in Burlington House at 10.30 a.m. on Friday, April 1st, 1955, the President, Professor W. Wardlaw, being in the Chair. After the notice convening the meeting had been read by Professor E. D. Hughes, Honorary Secretary, the President called upon Professor H. Burton, Honorary Secretary, to present the Report of Council for the year ended December 31st, 1954.

Professor Burton commented on the new subscription arrangements, introduced in 1955, and the closing of the Joint Subscription Scheme at the end of 1954. It was not possible at the present time to report fully on the effect of these changes upon the Fellowship of the Society.

The Society's *Journal* had increased substantially in size and the increased rate of receipt of new papers had continued. The present indications were that the receipts of new papers in 1955 would exceed those in 1952, the highest ever recorded in one year by the Society. The Society's new publication, *Current Chemical Papers*, had been well received and had become established in its first year. Full details of the scope and coverage of this publication were given in the Report. Professor Burton also referred briefly to the other activities of the Society mentioned in the Report. He expressed the thanks of the Society to all those who had assisted the Society in many ways, especially to those who had acted as referees to papers submitted for publication in the *Journal*. In conclusion, Professor Burton paid a tribute to the work of the Society's permanent staff during the past year.

The Accounts for 1954 were presented by the Honorary Treasurer. The balance of income over expenditure was satisfactory but somewhat precarious, since a small increase in the size of the *Journal* or in printers' charges could easily change the surplus into a substantial deficit. The ending of the Society's liability towards the Bureau of Abstracts had reduced the need for working capital and had enabled the Society to increase its investments on the General Purposes Fund and also on the Special Reserve Fund. At the same time, the proportion of investments outside the limited range of trustee securities had been increased. This policy should increase the investment income available to the Society and provide some measure of insurance against the continuing fall in the value of money.

He hoped that the new subscription arrangements which came into force on January 1st, 1955, would enable the Council to present the Society's Accounts in a more readily comprehensible manner. In particular it should be possible to show more clearly the profit or loss on each of the Society's publications. For 1954, however, he could report that *Annual Reports* and *Quarterly Reviews* both earned a satisfactory profit, the *Journal* was produced at a loss, and the new publication, *Current Chemical Papers*, had been self-supporting.

After discussion, the President moved the adoption of the Report of Council and the Accounts. This motion was seconded by Dr. L. E. Sutton, Honorary Secretary, and was carried unanimously.

The President then announced that the following had been elected to fill vacancies on the Council :

Honorary Secretary :

Professor F. Bergel.

Vice-Presidents who have not filled the Office of President :

Professor M. Stacey. Sir Alexander Todd.

Elected Ordinary Members of Council:

Constituency I:
Dr. D. W. Adamson.
Dr. A. W. Johnson.
Dr. W. Wild.
Dr. G. T. Young.

Constituency II:
Dr. F. H. Pollard.

Constituency III:
Dr. G. R. Barker.
Dr. A. Hickling.

Constituency V:
Professor F. Bell.

It was reported that, to fill the vacancy among the Ordinary Members of Council for Constituency I, caused by the appointment of Professor F. Bergel as Honorary Secretary, Council had, in accordance with Bye-Law 42, nominated Dr. A. Maccoll to serve for one year.

On the motion of the Honorary Treasurer and seconded by Dr. L. E. Sutton, Messrs. W. B. Keen and Co., Finsbury Circus House, London, E.C.2, were re-appointed as the Society's Auditors for 1955.

A vote of thanks to the President, Officers, Council, and Local Representatives, proposed by Sir Alexander Todd, who referred particularly to the services which the retiring Honorary Secretary, Professor H. Burton, had rendered to the Society, was carried with acclamation.

After an interval the meeting was resumed at 11.30 a.m. and the President presented the Corday–Morgan Medal and Prize for 1953 to Dr. J. W. Cornforth.

Professor W. Wardlaw then delivered his Presidential Address, "A Problem in Structural Chemistry." At the conclusion of the Address a vote of thanks, proposed by Professor C. K. Ingold, was carried with acclamation.

REPORT OF COUNCIL FOR 1954.

I. FELLOWSHIP.

1. *Honorary Fellowship.* The following were elected as Honorary Fellows of the Society on May 6th, 1954:

Jens Anton Christiansen.
Vincent du Vigneaud.

2. *General.* On December 31st, 1954 the number of Fellows of the Society totalled 9123. Fellowship changes during 1954 and previous years are given in the following Table:

TABLE 1.

	1951	1952	1953	1954
Number of Fellows on January 1st	8353	8616	9063	9249
Additions:				
Elections	700	947	790	670
Reinstatements	25	34	29	26
Miscellaneous	—	1	—	—
	— 725	— 982	— 819	— 696
Deductions:				
Deaths	62	65	58	71
Resignations	273	341	467	583
Removals	127	128	106	167
Miscellaneous	—	1	2	1
	— 462	— 535	— 633	— 822
Net change in year	+263	+447	+186	−126

Numbers participating in Joint Subscription Scheme:

Year	
1949	4615
1950	4797
1951	4823
1952	4837
1953	4407
1954	4185

3. *Joint Subscription Scheme.* As Fellows will be aware the Chemical Council have issued the following statement:

"The Chemical Council announces the cessation of the Joint Subscription Scheme at the end of 1954.

"It will be remembered that the scheme was instituted to afford those who were members at least of both the Chemical Society and the Society of Chemical Industry the opportunity of paying one subscription only which was somewhat less than the sum of the separate subscriptions to the several societies to which they belonged. It also gave a choice of publications which, though less than the full range offered by the societies, none the less satisfied the needs of many who were members of societies participating in the scheme.

"However, a subscriber who required publications in excess by more than £1 of the basic entitlement under the scheme derived no benefit and, moreover, all benefits have been much lessened by the rise in costs of publications during the last few years.

"From January 1st, 1955, the subscription structures of the Chemical Society and the Society of Chemical Industry, membership of both of which was essential for participating in the scheme, each become radically different, the Chemical Society having decided to alter its subscription to a basic one of two guineas without entitlement to any publications other than its *Proceedings*. The continued operation of the scheme is thus rendered impracticable.

"It will therefore be necessary for members who have been joint subscribers to pay their subscriptions in 1955 individually to the various societies to which they belong, and separate subscription renewal forms will be issued by each society."

It may be added that the closing of the Conjoint Chemical Office will, in future years, result in a significant saving of administrative costs for the Chemical Society.

4. *Congratulations.* The congratulations of the Society were conveyed to the following whose names appeared in the lists of Birthday and New Year Honours:

C.H.
John Christie.

K.B.E.
Lord Trent of Nottingham.

Knight Bachelor.
Alexander Robertus Todd.

C.B.E.
Harold Davies.
James Brierley Firth.
Walter Idris Jones.
Ernest Thomas Osborne.

The Council has also congratulated Professor Linus Carl Pauling (Honorary Fellow) on the award of the Nobel Prize for Chemistry, and also the following who received awards announced by the Royal Society:

Royal Medal.
Professor H. A. Krebs.

Davy Medal.
Professor J. W. Cook.

5. *Deaths.* The names of those Fellows whom the Society has lost by death have been announced in the *Proceedings*. By the passing on November 1st, 1954, of Sir Wallace Akers, the Council lost a friend and colleague who was greatly beloved by all those with whom he came into contact, and who, during his six years as Treasurer, rendered conspicuous service to the Society by his handling of its financial affairs.

The Council also report with deep regret the death, as a result of an accident, of John Theodore Hewitt (C. 1903—5, 1908—11, Vice-President 1922—25).

Obituary notices have been arranged.

II. PUBLICATIONS.

1. *Journal.* During 1954, 1019 scientific communications were received and 961 published. In comparison with 1953 (946 received, 866 published), these figures represent increases of 7 and 11% respectively. During 1954, 19 communications were declined and 30 were withdrawn. Table 2 shows some comparative figures.

TABLE 2.

	1938	1952	1953	1954
Papers and Notes received	507	1046	946	1019
Less rejected or withdrawn	11	59	52	49
	496	987	894	970
Papers and Notes published	404	1000	866	961
No. of pages (Papers and Notes)	1917	4901	4028	4552
No. of pages (total, excluding Index Volume)	2120	5056	4200	4712
Average no. of pages per communication	4·75	4·90	4·65	4·73

The number of communications received in recent years is shown in Table 3. From these figures it appears possible for the first time to assume that the post-war expansion has ceased and that the annual size of the *Journal* is becoming stabilised at about its present level of 900–1000 papers a year.

TABLE 3.

Numbers of Communications Received for Publication.

Year	1938	1944	1945	1946	1947	1948	1949	1950	1951	1952	1953	1954
Nos.	507	242	347	453	523	548	739	874	910	1046	946	1019

The *Journal* for 1954 contained 995 items made up as shown in Tables 4 and 5 where some comparative figures are also given.

TABLE 4.

Numbers of Items in the Journal.

	1938	1948	1951	1952	1953	1954
Papers (General, Physical, and Inorganic)	102	124	131	194	180	135
,, (Physical Organic)	—	16 *	100	134	93	125
,, (Organic)	275	326	462	556	492	581
Notes	27	45	85	116	101	120
Lectures and Addresses	9	5	3	6	6	7
Obituary Notices	37	17	9	21	14	22
Annual General Meeting	1	2	1	2	1	1
Extraordinary General Meeting	—	—	—	—	—	1
Bye-laws of the Chemical Society	—	—	—	—	—	1
Editorial Nomenclature Report	—	—	1	1	1	1
Report by Symbols Committee of the Royal Society	—	—	1	—	—	—
I.U.P.A.C. List of Atomic Wts.	1	—	1	—	1	1
,, Report of Commission of Nomenclature of Inorganic Chemistry	—	—	1	—	—	—
	452	535	795	1030	889	995

TABLE 5.

Percentage Distribution in the Journal.

	1948	1949	1950	1951	1952	1953	1954
Papers (General, Physical, and Inorganic)	20·3	16·9	18·4	16·8	19·4	20·8	14·0
,, (Physical Organic) *	3·1	14·4	13·8	12·8	13·4	10·8	13·0
,, (Organic)	63·8	60·9	58·7	59·4	55·6	56·7	60·5
Notes	8·8	7·8	9·1	10·9	11·6	11·7	12·5

* Class first introduced December 1948.

Contributions from industrial laboratories and industrial research organisations published during 1954 totalled 126, including 13 published jointly with academic institutions and 3 jointly with Government organisations; this represents 13·1% of the total. Contributions from Government sources totalled 47, including 6 jointly with academic institutions and 3 jointly with industrial organisations. Communications from overseas published during 1954 numbered 194 (20·2%) (1952, 15·7%; 1953, 16·2%). The proportions of contributions from overseas and from non-academic sources thus continued their previous increases. Table 6 gives details of the contributions from overseas, those published jointly with British laboratories being shown in parentheses.

TABLE 6.

	1948	1951	1952	1953	1954
Australia	13	38(1)	62(1)	50	62(2)
British Colonies and Protectorates	—	4(1)	6(3)	5(1)	9(2)
Canada	2	1	2(1)	2	6(1)
Egypt	15	22	12	8	16
France	2	10	10	7	8(2)
Hungary	6	1	3	7	0
India and Pakistan	3	3	3(1)	6	13
Irish Republic	—	5	4	5	5
Israel	2	7	10(2)	20	15
Italy	—	—	—	—	9
New Zealand	14	5	18	12(1)	14(1)
South Africa	1	10	14(1)	7	8(1)
U.S.A.	2	13(7)	8(3)	7(1)	24(3)
Miscellaneous	7	2(1)	5	4(1)	5(1)
	67	121(10)	157(12)	140(4)	194(13)

The number of communications received during 1954 less the number rejected or withdrawn was 970; the number published during the year was 961. An analysis has shown that the normal time, to the nearest week, between receipt of communications and their publication (taken as the first day of the following month) is 22 weeks.

2. *Annual Reports on the Progress of Chemistry for* 1953 (*Volume L*). These were issued in July 1954 and contained 378 pages (381 in 1953, and 428 in 1952, but this comparison is not quite valid, since a new format with more text per page was adopted in the *Reports* for the current year). To celebrate the half-century a foreword was written by Sir Cyril Hinshelwood.

3. *Quarterly Reviews*. Volume VIII (1954) contained 17 articles occupying 450 pages (Volume VII, 16 articles, 443 pages). A Cumulative Index of Authors and a short Cumulative Index of Subjects was, for the first time, included at the end of the volume.

4. *Current Chemical Papers*. This new publication bears the sub-title "A classified world list of new papers in pure chemistry."

Each issue of every journal received in the Society's Library is scanned immediately on receipt, and the titles of all the papers adjudged to contain original work in pure chemistry, together with those of outstanding reviews, are extracted for the forthcoming issue of *Current Chemical Papers*. This is distributed on the Wednesday nearest to the middle of each month, and the papers listed in that issue were received in the Society's Library during the preceding calendar month.

Thus any paper listed may at once be consulted in the Society's Library; and the Society's photocopying service is available to Fellows of the Society and to members of other Bodies entitled to use the Library.

During 1954 the papers were classified in *Current Chemical Papers* under sixteen sections, and within each section were arranged by principal subjects. When the paper was of primary interest in more than one section, entries were replicated. As a result of the year's experience, the number of sections has been raised to twenty for 1955.

Each entry states the title of the paper (in English), expanded when necessary to

indicate the subject matter, followed by the authors' names and the full journal reference. When the language is not that to be expected from the title of the journal, the language is also given; for Swiss, Dutch, and international journals the language is named if it is other than English, German, or French. For papers in languages other than English, German, or French, any summary in one of those three languages is also mentioned.

A list of the journals covered was included with the April 1954 issue, and a supplementary list with the July 1954 issue. A complete list (containing further additions) is included in the January 1955 issue, where also are given the abbreviations used (these abbreviations differ in some cases from those used by the Society up to 1954, and the new styles will be used also in the Society's other publications).

It is believed that *Current Chemical Papers*, which brings its information more promptly than is possible for an abstract journal, is of value to research workers; but it is intended to supplement rather than to replace abstracts, and no index is issued.

Starting in January 1955, an edition on air-mail paper and also an edition printed only on one side of the paper are available.

Table 7 gives some statistics for *Current Chemical Papers* for the year 1954.

TABLE 7.

Current Chemical Papers, 1954.

	Totals.	Average per issue.
Titles of papers listed	19,531	1628
Issues of journals yielding titles	2,006	167
Journals yielding titles	325	129
Pages (of *C.C.P.*)	633	53
Issues of journals not yielding titles	—	137
Total number of journals scanned	437	—

The journals, totalling 437 in December 1954, are believed to include almost all which contain original work in pure chemistry, though additions are continually under investigation. However, only ten Russian journals are received in the Library at present; although these ten cover the great bulk of Russian chemistry, it is hoped that this number will be increased shortly. Coverage of the German literature was not complete at the beginning of the year, but it is believed that by the end of 1954 very little pure chemistry from Germany was being missed.

U.S. translations were included for the older issues of Russian journals not previously cited in *Current Chemical Papers*; when the U.S. translation was received of a Russian journal already included in *Current Chemical Papers*, its receipt was recorded in *Current Chemical Papers*, together with a back-reference to the issue containing the titles from the original Russian.

The figures in Tables 8 and 9, abstracted from the records of *Current Chemical Papers*, may have wider interest. Table 8 gives the numbers of papers, and percentages, classified according to the country in which the journals were published. The Russian figure is swollen by inclusion in it of a backlog of work from a supplement to *Zhurnal obschei Khimii* received in 1954, but this is offset by the incomplete coverage referred to above. The Japanese figures are swollen by duplicate publication in Japanese and English or German. Further, Table 8 does not give a completely accurate picture of the countries of origin of the work; for instance, 20% of the papers in the Society's *Journal* in 1954 contained work done wholly or partly overseas, including 11·25% in other countries of the Commonwealth; the latter figure alone, representing 112 papers, materially increases that in Table 8 of 311 papers; similarly, papers in the Society's *Journal* alone from Israel (15) are nearly double the figure (8) for that country in Table 8. Nor, of course, is the mere number of papers a true indication of their volume, and far less of their value. Nevertheless, in spite of these reservations, some *prima facie* value is doubtless attached to the figures in Table 8; they show at least which countries carry the onus of publication, and give a rough indication of their relative contributions to pure chemistry.

TABLE 8.

Papers in C.C.P., 1954, *classified according to the country in which the original journal was published.*

	Nos.	%.
U.S.A.[1]	6,104	32·54
U.K.	2,625	13·94
Germany [2]	1,889	10·02
U.S.S.R.[3]	1,760	9·35
Japan [4]	1,653	8·78
France	1,113	5·91
Netherlands	509	2·70
Scandinavia	494	2·62
India	443	2·35
Italy	393	2·09
Czechoslovakia [5]	328	1·74
British Commonwealth (other than the U.K. and India)	311	1·65
Switzerland	297	1·58
Spain and Portugal	257	1·37
Hungary	174	0·93
Poland	166	0·89
Jugoslavia	94	0·50
Austria	81	0·43
Belgium	45	0·24
Latin America	50	0·27
Turkey	12	0·06
Israel	8	0·04
	18,806	100·00

Notes: (1) U.S.A. does not include U.S. translations of Russian journals. (2) Germany, slightly too low (correct figure probably nearer 11%), owing to incomplete coverage early in the year. (3) U.S.S.R., too low, owing to incomplete coverage. (4) Japan, much too high (correct figure nearer 6—7%), owing to duplicate publication in Japanese and English or German. (5) Much too high (correct figure probably nearer 1·0%), owing to duplication between *Chem. Listy* (in Czech) and *Coll. Czech Chem. Comm.* (in English, German, or French).

Table 9 gives the approximate percentages of the languages in which papers contained in *Current Chemical Papers* were written.

TABLE 9.

Language used in papers included in C.C.P., 1954—*Approximate Percentages.*

English	59·5
German	13·2
Russian	9·4
French	7·1
Japanese	4·4
Italian	2·1
Spanish and Portuguese	1·6
Czech	0·9
Hungarian	0·5
Polish	0·5
Others	0·8
	100·0

5. *Special Publication No.* 1. A new range of publications, called " Special Publications," has been sanctioned, to include collations of data, reports of symposia, or other chemical material which, in the opinion of Council, merit publication by the Society but do not find their place in any of the Society's other publications. The first of the series, *The Kinetics and Mechanism of Inorganic Reactions in Solution: A Survey of Recent Work*, was published on November 2nd, 1954. It is a report of a symposium held in the Society's rooms on February 4th, 1954, and organised by Dr. L. E. Sutton and Dr. J. Chatt. Dr. K. W. Sykes was Specialist Editor for this report, which occupied 84 pages, similar in size to those of *Quarterly Reviews*.

III. MEETINGS.

1. *Scientific Meetings.* Details of Scientific Meetings held in London and those arranged at various centres by Local Representatives of the Society are given in Appendix A. The meetings in London included a Conversazione held at the Senate House on May 7th.

2. *Anniversary Meetings.* The Anniversary Meetings were held in Manchester on March 31st to April 2nd.

3. *Centenary Lectures.* Dr. R. H. Manske delivered a Centenary Lecture, entitled "The Story of the *iso*Quinoline Alkaloids," in London, Edinburgh, Liverpool, Newcastle, and St. Andrews.

IV. LIBRARY.

1. *Report of the Joint Library Committee.* This is reproduced as Appendix B.

2. *Appointment of Librarian.* The Council received with great regret the resignation of Mr. A. E. Cummins on grounds of ill health from the appointment of Librarian. To mark the services he has rendered to the Society and to all who have used the Library the Council has arranged for a presentation to be made to Mr. Cummins.

To fill the vacancy the Council has appointed Mr. R. G. Griffin, formerly Librarian at the Brewing Industry Research Foundation, as Librarian.

V. OTHER ACTIVITIES.

1. *Grants for Research.* Grants from the Research Fund totalling £744 10s. were made to thirty-two applicants.

2. *Longstaff Medal.* The Longstaff Medal for 1954 was awarded to Sir John Lennard-Jones.

3. *Flintoff Prize.* The first award of the Flintoff Prize was made to Professor M. Calvin.

4. *Corday–Morgan Medal and Prize.* The Corday–Morgan Medal and Prize for 1952 was awarded to Dr. J. Baddiley.

5. *Harrison Memorial Prize.* The Harrison Memorial Prize for 1953 was awarded to Dr. R. J. Gillespie.

6. *Corday–Morgan Memorial Fund Executive.* The Corday–Morgan Memorial Fund Executive have reported that the Corday–Morgan Commonwealth Fellowship for 1954—55 has been awarded to Dr. L. E. Smythe, University of Tasmania.

7. *Royal Horticultural Society.* Sir John Simonsen represented the Society at the 150th Anniversary Meetings on July 27th and presented an Address.

VI. ADMINISTRATION.

1. *Council.* At the Annual General Meeting on April 2nd, the following were declared elected :

President	Professor W. Wardlaw.
Vice-Presidents who have not filled the Office of President	Professor E. R. H. Jones, Professor R. P. Linstead, Professor H. W. Melville.
Honorary Treasurer	Mr. M. W. Perrin.
Elected Ordinary Members of Council	Dr. C. C. Addison, Dr. V. C. Barry, Dr. E. J. Bourne, Dr. E. A. Braude, Dr. H. M. N. H. Irving, Professor J. M. Robertson, Professor H. N. Rydon, Professor H. D. Springall.

2. *Local Representatives.* The following have been elected to fill vacancies among the Society's Local Representatives :

Birmingham	Dr. J. C. Tatlow in place of Dr. E. J. Bourne.
Bristol	Dr. P. Woodward in place of Dr. F. H. Pollard.
Glasgow	Dr. D. S. Payne in place of Dr. F. D. Gunstone.
Hull	Dr. G. W. Gray in place of Dr. W. B. Orr.
Irish Republic	Dr. D. O'Tuama in place of Dr. V. C. Barry.
Leeds	Dr. E. Rothstein in place of Dr. P. A. Briscoe.
Oxford	Mr. L. A. K. Staveley in place of Dr. H. M. N. H. Irving.
St. Andrews and Dundee	Dr. C. Horrex in place of Dr. H. T. Openshaw.

VII. FINANCE.

1. *Accounts.* The Accounts for the year under review reflect the continuing improvement in the financial position of the Society, and it is gratifying to report that this is the first time for many years that the Society has been able to show a surplus in its accounts without the assistance of outside support. In part, of course, this is due to the cessation of payments to the Bureau of Abstracts which were balanced by outside support, but it can also be attributed to the increased selling price of the Society's publications. Notwithstanding the relatively satisfactory position at the end of 1954, it would be well to record that the Society's expenditure is governed by the size of its *Journal*, and that a relatively small increase in the number of pages could easily turn a small surplus into a substantial deficit.

It is a matter of satisfaction that the Society's new publication, *Current Chemical Papers*, has been self-supporting in 1954. This publication fulfils some of the functions of *British Chemical Abstracts " A "*.

Changes in the major items of income and expenditure over the past seven years are given in Table 10.

TABLE 10.

	Income.			*Expenditure.*		
	Annual subscriptions (net).	Sale of publications.	Outside grants.	Administration.	Journal of the Society.	Contributions to Bureau of Abstracts.
	£	£	£	£	£	£
1948	20,745	9,503	3,400	7,855	19,997	5,300
1949	22,629	13,778	5,233	7,492	31,963	5,300
1950	26,884	16,784	15,984	7,468	31,713	12,084
1951	26,928	22,358	33,500 *	7,632	36,309	14,000
1952	29,273	21,365	49,550	7,178	53,439	26,000
1953	38,801	30,231	20,100	7,619	44,542	17,800
1954	39,111	32,926	Nil	7,788	46,535	Nil

* Includes £9500 in respect of previous years.

2. *Library.* The thanks of the Council have been accorded to the Chemical Council for a grant of £821 11*s.* 10*d.* towards the maintenance costs of the Library and also to those Societies who have continued to contribute on a membership basis in return for the use of the Library by their members.

3. *Investments.* Council has authorised the investment of part of the balances held on the General Purposes Fund and Special Reserve Fund Accounts which were no longer required as working capital. The apportionment of the Society's investments between the different categories of trustee and non-trustee investments has also been reviewed, and various changes have been authorised. The net result of these and of small changes on the other funds is given in the Schedule of Investments appended to this Report. The additional investments should considerably increase the investment income in future years.

4. *A. G. Perkin Bequest.* The bequest made to the Society under the Will of the late Professor A. G. Perkin has become payable. It amounts to £4305 19*s.* 5*d.*, one-fifth of the residuary estate, and the Society is directed to invest the capital and to apply the income to the general purposes of the Society. The testator expressed the wish that the income should, so far as it could conveniently be done, be applied for the purpose of reducing the expense incurred in the publication of the *Journal*.

VIII. REPRESENTATIVES OF THE SOCIETY ON OTHER BODIES.

In 1954 the Society was represented on various bodies by the following :

" Acta Metallurgica " :

International Journal of the Science of Metals : Dr. U. R. Evans.

Association of British Chemical Manufacturers :

Joint Technical Committe on Patents : Dr. J. T. Hewitt.

Barker Committee :

Formed to support the publication of the Barker Index of the characteristic angles of crystalline compounds : Dr. G. M. Bennett.

Bristol University Court :

Professor C. E. H. Bawn.

British National Committee for Chemistry :

Sir Eric Rideal, Professor E. D. Hughes, Professor M. Stacey.

British National Committee for Crystallography :

Professor J. M. Robertson.

British Standards Institution. Technical Committees :

C/17.	Viscosity : Dr. A. E. Dunstan.
C/34.	Standardization of pH Scale : Professor H. T. S. Britton.
CHE/36.	Chemicals and Chemical Plant for Electroplating : Dr. J. R. I. Hepburn.
DAC/-.	Dairying Industry Standards Committee : Mr. Eric Voelker.
FCC/HCC/1.	Nomenclature for Fine and Heavy Chemicals Industries : The Editor.
HCC/2.	Desiccants : Dr. B. Lambert.
LBC/-.	Scientific Glassware and Related Laboratory Apparatus, Industry Standards Committee : Dr. G. R. Davies.
LBC/1/1.	Dean and Stark and Ubbelohde Apparatus : Dr. G. R. Davies.
LBC/5.	Hydrometers : Mr. R. Sutcliffe.
LBC/6.	Standard Distillation Apparatus : Mr. R. Sutcliffe.
LBC/11.	Microchemical Apparatus : Dr. R. Belcher, Dr. H. D. K. Drew.
LBC/11/1.	Apparatus for Microchemical Combustion Methods : Dr. R. Belcher.
LBC/11/3.	Accessory Apparatus connected with Gravimetric Microanalysis : Dr. R. Belcher.
LBC/16.	Standardization of Glass Electrodes : Dr. D. J. G. Ives.
LBC/16/2.	Drafting Work on pH Meters : Dr. D. J. G. Ives.
LBC/17.	Apparatus Drawing Conventions : The Editor.
LBC/18.	Laboratory Furniture and Fittings : Mr. R. Sutcliffe.
LGE/19.	Colour Terminology : Dr. F. M. Hamer.
PAC/13.	Filter Papers : Mr. F. H. Burstall.
PAC/13/1.	Laboratory Filter Paper (Drafting) : Mr. F. H. Burstall.
PCC/1.	Nomenclature for Pest Control Products : The Editor.
RUC/8.	Rubber Tubing and Bungs for Laboratory Use : Dr. L. C. Bateman.
USM/1.	Co-ordination of Definitions, Units and Technical Date : The Editor.
USM/1/2.	Glossary of Terms used in Nuclear Sciencies : The Editor.
USM/2.	Abbreviations and Symbols : The Editor.
USM/2/2.	Abbreviations and Letter Symbols (Chemical Engineering and Applied Chemistry) : The Editor.

Bureau of Abstracts. Continuing Committee :

Sir Wallace Akers, Dr. G. M. Bennett, Dr. G. M. Dyson, Professor H. Burton.

Chemical Council :

The Honorary Treasurer, Professor C. K. Ingold, Professor E. D. Hughes, Dr. L. E. Sutton.

City and Guilds of London Institute :

The President.

Faraday Society. Colloid and Biophysics Committee :

Dr. G. L. Riddell.

Joint Library Committee :

Professor D. H. R. Barton, Dr. L. C. Bateman, Dr. J. H. Burgoyne, Professor M. J. S. Dewar, Dr. J. E. Garside, Dr. J. Kenyon, Professor K. Lonsdale, Dr. A. Maccoll, Dr. J. W. Smith, Dr. L. E. Sutton, Professor C. Tyler, Professor R. L. Wain, Dr. J. Walker, Professor W. Wardlaw.

Lawes Agricultural Trust. Committee of Management :

Sir John Simonsen.

Parliamentary and Scientific Committee :

The President, The General Secretary.

Regional Council for Further Education for the South-West. Chemistry and Chemical Technology Committee :

Professor W. E. Garner.

Royal Society. Joint Standing Committee for Symbols and Abbreviations :

Mr. R. P. Bell, The Editor.

Royal Society. Scientific Societies Accommodation Committee :

The President.

Society of Dyers and Colourists. Perkin Centenary Committee :

Dr. M. A. T. Rogers.

Yorkshire Council for Further Education. Advisory Committee for Chemistry in South and East Yorkshire :

Professor R. D. Haworth.

APPENDIX A.

MEETINGS HELD DURING 1954.

IN LONDON.

(Meetings were held in the Rooms of the Society at Burlington House unless otherwise stated.)

January 21st, *Meeting* for the reading of original papers; February 4th, *Symposium*, " Kinetics and Mechanism of Inorganic Reactions in Solution. A Survey of Recent Work," arranged by Dr. L. E. Sutton and Dr. J. Chatt (contributions from the following were read and discussed: Dr. A. W. Adamson, Dr. J. H. Baxendale, Professor F. S. Dainton, Dr. R. Hurst, Professor C. K. Ingold, Dr. H. M. N. H. Irving, Dr. K. W. Sykes, and Dr. R. G. Wilkins); February 18th, *Meeting* for the reading of original papers; March 25th, *Liversidge Lecture*, " Organometallic Compounds containing Fluorocarbon Radicals," by Professor H. J. Emeléus; May 6th, *Centenary Lecture*, " The Story of the *iso*Quinoline Alkaloids," by Dr. R. H. Manske; May 7th, *Reception and Conversazione*, at The Senate House, University of London, W.C.1. (by kind permission of the University authorities); June 3rd, *Hudson Memorial Lecture*, by Professor E. L. Hirst; October 14th, *Meeting* for the reading of original papers; November 4th, at the Imperial College of Science and Technology, *Lecture*, " On Open and Closed Sequences in Reaction Kinetics," by Professor J. A. Christiansen (*Honorary Fellow*); November 18th, at the Imperial College of Science

and Technology, *Tilden Lecture,* " Molecular Rearrangements," by Professor M. J. S. Dewar; December 2nd, *Meeting* for the reading of original papers; December 16th, *Hugo Müller Lecture,* " Some Newer Aspects of the Organic Chemistry of Nitrogen," by Professor G. R. Clemo.

OUTSIDE LONDON

Aberdeen. Joint meetings with the Royal Institute of Chemistry and the Society of Chemical Industry, at Robert Gordon's Technical College: January 21st, *Lecture,* " New Outlooks in Electrochemistry," by Professor W. F. K. Wynne-Jones; February 18th, *Lecture,* " The Scientific Examination of Paintings," by Dr. A. E. Werner; March 5th, *Lecture,* " Recent Advances in Carotenoid Chemistry," by Dr. T. W. Goodwin; April 1st, *Lecture,* " Some Aspects of the Newer Techniques in Analytical Chemistry," by Dr. J. R. Nicholls; October 21st, *Lecture,* " Some Aspects of the Chemistry of Amino-sugars," by Professor M. Stacey; December 10th, *Lecture,* " Terylene," by Mr. J. R. Whinfield.

Birmingham. Joint meetings with the University Chemical Society, at the University: January 22nd, *Lecture,* " Aromatic Substitution," by Professor M. J. S. Dewar; March 12th, *Lecture,* " Friction and Lubrication," by Dr. D. Tabor; October 22nd, *Lecture,* " Some Recent Advances in the Stereochemistry of Polycyclic Hydroaromatic Compounds," by Dr. J. Walker; November 19th, *Lecture,* " The Structure and Properties of Olefin Complexes," by Dr. J. Chatt; December 3rd, *Lecture,* " Some Aspects of the Organic Chemistry of Phosphorus," by Professor H. N. Rydon.

Bristol. Joint meetings with the Royal Institute of Chemistry and the Society of Chemical Industry, at the University, unless otherwise stated: January 14th, *Lecture,* " Cacao Diseases," by Mr. R. V. Wadsworth; January 21st, *Lecture,* " Some New Methods in Analytical Chemistry," by Dr. R. Belcher; February 4th, *Lecture,* " The Radiochemical Centre at Amersham," by Dr. W. P. Grove; February 17th, at the Technical College, Gloucester, *Lecture,* " The Use of Radiochemical Methods in Analysis," by Mr. A. Smales; March 4th, also joint with the Institute of Fuel, *Lecture,* " National Fuel Resources and their Utilisation," by Dr. A. Parker; March 18th, *Lecture,* " Patent Specifications regarded as Chemical Literature," by Dr. W. A. Sylvester; October 7th, *Lecture,* " Sulphur and Sulphuric Acid from Petroleum," by Mr. F. E. Hixon; October 13th, also joint with the Plastics Institute, at the Technical College, Gloucester, *Lecture,* " Some Newer Plastics and their Uses," by Dr. G. Darnton; October 28th, *Lecture,* " Some Recent Advances in Fluorine Chemistry," by Professor H. J. Emeléus; November 4th, *Lecture,* " Melting and Crystal Structure," by Professor A. R. Ubbelohde; November 11th, at the Technical College, Gloucester, *Lecture,* " Plant Growth Substances—Some Recent Developments," by Professor R. L. Wain; November 18th, *Social Evening*; December 2nd, also joint with the Institute of Metals and the Chemical Engineering Group of the Society of Chemical Industry, *Lecture,* " The Thermochemistry of Alloys," by Dr. A. R. Harding.

Cambridge. Joint meetings with the University Chemical Society, at the Chemical Laboratory, Pembroke Street; January 29th, *Lecture,* " The Chemical Society, Present and Future," by Dr. R. S. Cahn; February 5th, *Lecture,* " Reactions in Liquid Dinitrogen Tetroxide," by Dr. C. C. Addison; March 5th, *Lecture,* " Azaporphyrins," by Professor R. P. Linstead; October 29th, *Lecture,* " Gas–Liquid Chromatography," by Dr. A. J. P. Martin; November 5th, *Lecture,* " Some Mould Colouring Matters," by Professor A. Robertson; December 3rd, *Lecture,* " The Polymerisation of Vinyl Ethers," by Professor D. D. Eley.

Edinburgh. Joint meetings with the Royal Institute of Chemistry and the Society of Chemical Industry, held at the North British Station Hotel, unless otherwise stated: January 14th, *Lecture,* " The Stereochemistry of *cyclo*Hexane Derivatives," by Professor D. H. R. Barton; February 2nd, also joint with the University Chemical Society, at the Biochemistry Lecture Theatre, Teviot Place, *Lecture,* " New Kinds of Big Molecules," by Professor H. W. Melville; February 18th, *Lecture,* " Recent Progress in the Study of Metallic Corrosion," by Dr. W. H. J. Vernon; March 18th, *Meeting* for the reading of original papers; April 27th, in the Medical Building, Teviot Place, *Official Meeting and*

Centenary Lecture, "The Story of the *iso*Quinoline Alkaloids," by Dr. R. H. Manske; October 14th, *Lecture*, "Chemical Research at Harwell," by Dr. R. Spence; November 11th, *Visit* to the Research Laboratories of the University Chemistry Department; December 9th, *Lecture*, "Recent Researches in Crystallography," by Professor Kathleen Lonsdale.

Exeter. At the Washington Singer Laboratories, unless otherwise stated: February 12th, joint meeting with the Royal Institute of Chemistry, *Lecture*, "The Chemical Effects of Nuclear Transformations," by Dr. A. G. Maddock; March 5th, joint meeting with the Royal Institute of Chemistry and the Society of Chemical Industry, at the Technical College, Plymouth, *Lecture*, "Rubber," by Dr. C. M. Blow; March 9th, *Tilden Lecture*, "Aromatic Character in Seven-membered Ring Systems," by Dr. A. W. Johnson; November 26th, *Lecture*, "Some Applications of Electron Diffraction to Problems in Inorganic Chemistry," by Dr. L. E. Sutton; December 17th, *Lecture*, "There and Back again; Some Aspects of the Problem of Hysteresis," by Professor D. H. Everett.

Glasgow. January 22nd, at the Royal Technical College, *Lecture*, "The Investigation of Natural Products derived from Wood," by Professor F. E. King; February 19th, at the University, Annual General Meeting of local Fellows followed by a *Meeting* for the reading of original papers; October 22nd, joint meeting with the Alchemists' Club and the Andersonian Chemical Society, at the University, *Lecture*, "Some Recent Advances in Carbohydrate Chemistry," by Professor M. Stacey; November 19th, at the Royal Technical College, *Lecture*, "The Chemical Nature of Some Metal Alkyls," by Professor G. E. Coates.

Hull. At the University: January 21st, joint meeting with the Royal Institute of Chemistry, *Lecture*, "Proteins and Plastics," by Professor J. C. Speakman; February 18th, joint meeting with the University College Scientific Society, *Lecture*, "Allene Chemistry," by Professor E. R. H. Jones; October 21st, *Lecture*, "The Work of the British Rubber Producers' Research Association," by Dr. L. C. Bateman; December 9th, joint meeting with the Royal Institute of Chemistry, *Lecture*, "Chemotherapy and Essential Trace Elements," by Professor A. Albert.

Irish Republic. January 27th, at Trinity College, Dublin, *Lecture*, "Studies in the Chemistry of Flavones," by Professor T. S. Wheeler; March 23rd, March 24th, and March 26th, joint meetings with the Institute of Chemistry of Ireland, the Royal Institute of Chemistry and the Society of Chemical Industry, held at Cork, University College, Dublin, and University College, Galway, respectively, *Lecture*, "Some Aspects of Oligo and Polysaccharide Synthesis," by Dr. E. J. Bourne; April 7th, joint meeting with the Institute of Chemistry of Ireland, the Royal Institute of Chemistry, and the Society of Chemical Industry, at University College, Dublin, *Lecture*, "The Steric Course of Asymmetric Synthesis," by Professor Dr. V. Prelog; May 7th, joint meeting with the Werner Society, at Trinity College, Dublin, *Lecture*, "Past, Present, and Future in Theoretical Chemistry," by Professor C. A. Coulson; December 8th, at University College, Dublin, *Lecture*, "Paul Ehrlich, 1854—1915," by Dr. J. G. Belton.

Leeds. At the University: January 18th, *Royal Institute of Chemistry Lecture*, "The Naturally Occurring Polyacetylenes," by Professor B. Lythgoe; February 15th, *Royal Institute of Chemistry Lecture*, "Corrosion Theory in Practice," by Dr. T. P. Hoar; March 9th, joint meeting with the University Chemical Society, *Lecture*, "The Stereochemistry of *cyclo*Hexane Derivatives," by Professor D. H. R. Barton; March 15th, *Royal Institute of Chemistry Lecture*, "Chemistry, Biochemistry, and Isotopic Tracer Technique," by Dr. G. J. Popjack; October 26th, joint meeting with the University Chemical Society, *Royal Institute of Chemistry Lecture*, "Polyester Fibres and Terylene," by Dr. R. Hill; November 2nd, *Lecture*, "The Mechanism of Some Electron-transfer Reactions," by Professor C. E. H. Bawn; November 22nd, *Royal Institute of Chemistry Lecture*, "The Lotoflavin Problem; the Study of a Toxic Natural Product," by Professor T. S. Wheeler; December 13th, joint meeting with Bradford Chemical Society, at Bradford, *Royal Institute of Chemistry Lecture*, "Configuration and Properties of Polymer Molecules in Dilute Solution," by Professor P. J. Flory. Fellows were invited to all meetings of the Royal Institute of Chemistry, Leeds Area Section, as well as to those organised by other bodies.

Liverpool. Joint meetings with the University Chemical Society, the Royal Institute of Chemistry, the Society of Chemical Industry, and the British Association of Chemists,

at the University: January 21st, *Lecture*, "Fluorescence," by Dr. E. J. Bowen; March 25th, *Lecture*, "The Biochemistry of Adrenocortical Hormones," by Professor G. F. Marrian; April 23rd, *Centenary Lecture*, "The Story of the *iso*Quinoline Alkaloids," by Dr. R. H. Manske; October 28th, *Lecture*, "Chemisorption and Catalysis," by Dr. F. C. Tompkins; December 2nd, *Lecture*, "Macrozamin and the Aliphatic Compounds," by Professor B. Lythgoe.

Manchester. At the University: January 28th, joint meeting with the Royal Institute of Chemistry and the Society of Chemical Industry, *Lecture*, "Polymerisation and its Reversal," by Professor F. S. Dainton; February 25th, *Lecture*, "Some Problems in the Chemistry of Polypeptides," by Professor H. N. Rydon; March 31st, joint meeting with the Royal Institute of Chemistry, the Society of Chemical Industry, and the Institute of Petroleum *Symposium*, "Dynamic Stereochemistry" (contributions from the following were read and discussed: Professor K. Alder, Professor D. H. R. Barton, Professor E. D. Hughes, Dr. P. B. de la Mare, Professor Dr. V. Prelog, and Professor S. Winstein); March 31st to April 2nd, *Anniversary Meetings*; October 1st, joint meeting with the Royal Institute of Chemistry and the Society of Chemical Industry, *Lecture*, "Some Aspects of Research on Plant Growth-regulating Substances," by Professor R. L. Wain; November 11th, *Meeting* for the reading of original papers; December 2nd, joint meeting with the Institute of Physics, *Lecture*, "Configuration and Properties of Polymer Molecules in Dilute Solution," by Professor P. J. Flory.

Newcastle and Durham. At King's College, Newcastle-on-Tyne: January 15th, *Bedson Club Lecture*, "Biochemistry and Parasitism," by Professor E. Baldwin; February 26th, *Bedson Club Lecture*, "Adhesion and Surface Properties of Solids," by Dr. F. P. Bowden; April 30th, *Centenary Lecture*, "The Story of the *iso*Quinoline Alkaloids," by Dr. R. H. Manske. Joint Meetings with the Durham Colleges Chemical Society at the University, Durham: October 11th, *Lecture*, "Recent Developments in Radiation Chemistry," by Dr. N. Miller; October 25th, *Lecture*, "Chemical Microscopy," by Dr. N. H. Hartshorne. At King's College, Newcastle-on-Tyne: October 29th *Bedson Club Lecture*, "Some Physicochemical Studies on π-Electron Compounds," by Professor A. R. Ubbelohde; November 12th, *Bedson Club Lecture*, "The Comparative Organic Chemistry of Nitrogen, Phosphorus and Arsenic," by Dr. F. G. Mann. At the University, Durham: November 24th, joint meeting with the Royal Institute of Chemistry and the Society of Chemical Industry, *Lecture*, "The Molecular Structure of Benzene, Some Unsolved Problems," by Professor E. G. Cox; November 29th, joint meeting with the Durham Colleges Chemical Society, *Lecture*, "Some Aspects of the Chemistry of Amino-sugars," by Professor M. Stacey; at King's College, Newcastle-on-Tyne, December 3rd, *Meeting* for the reading of original papers.

Northern Ireland. At Queen's University, Belfast: February 17th, joint meeting with the Society of Chemical Industry, *Lecture*, "Krilium Soil Conditioner," by Dr. A. J. Lloyd; March 5th, joint meeting with the Royal Institute of Chemistry, *Lecture*, "Chemical Engineering and Industrial Productivity," by Professor D. M. Newitt; April 5th, *Lecture*, "The Steric Course of Asymmetric Synthesis," by Professor Dr. V. Prelog; April 22nd, *Meeting* for the reading of original papers; May 7th, *Lecture*, "Oxidation in Aqueous Solution," by Dr. J. W. Baxendale; joint meetings with the Royal Institute of Chemistry and the Society of Chemical Industry: September 6th, *Lecture*, "Spot Test Methods of Analysis," by Professor P. W. West; October 14th, *Lecture*, "The Production and Properties of Titanium and Titanium Alloys," by Dr. N. P. Inglis; November 1st, *Lecture*, "The Polymerisation of Sulphur," by Professor G. Gee.

North Wales. Joint meetings with the University College of North Wales, Chemical Society, at the University College of North Wales, Bangor: March 18th, *Lecture*, "Some Problems in the Chemistry of Polypeptides," by Professor H. N. Rydon; May 6th, *Lecture*, "Atoms and Molecules in Cages," by Mr. H. M. Powell; October 21st, *Lecture*, "Electronic Mechanisms of Oxidation," by Dr. W. A. Waters.

Nottingham. Joint meetings with the University Chemical Society, at the University, unless otherwise stated: January 25th, joint meeting with Leicester University College Chemical Society, at University College, *Lecture*, "Some Recent Progress in Natural-product

Chemistry," by Professor D. H. R. Barton; January 28th, *Lecture*, " Structures and Configurations," by Professor E. E. Turner; February 9th, *Lecture*, " Recent Advances in the *X*-Ray Study of Complex Molecules," by Professor J. M. Robertson; February 25th, *Lecture*, " The Modern Theory of Aromatic Substitution," by Professor H. C. Longuet-Higgins; October 14th, *Lecture*, " Direct Hydroxylation of Organic Compounds," by Professor W. Bradley; October 18th, joint meeting with Leicester University College Chemical Society, at the University College, *Lecture*, " The Stereochemistry of Catalytic Hydrogenation," by Professor R. P. Linstead; November 25th, *Lecture*, " Mould Colouring Matters," by Professor A. Robertson.

St. Andrews and Dundee. January 15th, at the United College, St. Andrews, *Royal Institute of Chemistry Lecture*, " Recent Advances in Inorganic Chromatography," by Dr. F. H. Pollard; February 5th, joint meeting with the St. Andrews University Chemical Society, at the United College, *Lecture*, " Atoms and Molecules in Cages," by Mr. H. M. Powell; February 11th, at University College, Dundee, *Lecture*, " The Structure of Flames," by Dr. J. W. Linnett; February 19th, joint meeting with the St. Andrews University Chemical Society, at the United College, *Lecture*, " Some Naturally Occurring Polyacetylenes," by Professor B. Lythgoe; February 19th, at University College, Dundee, *Royal Institute of Chemistry Lecture*, " The Sterols—Their Chemistry and Metabolism," by Dr. R. P. Cook; February 25th, at University College, Dundee, *Chemistry Department Lecture*, " Steel," by Sir Charles Goodeve; February 26th, joint meeting with St. Andrews University Chemical Society, at United College, *Lecture*, " The Structure and Properties of Synthetic Polypeptides," by Dr. C. H. Bamford; March 4th, at University College, Dundee, *Society of Chemical Industry Lecture*, " Recent Developments in Carotenoid Biochemistry," by Dr. T. W. Goodwin; March 19th, at University College, Dundee, *Royal Institute of Chemistry Lecture*, " Technical Education," by Professor H. B. Nisbet; April 16th, at University College, Dundee, *Royal Institute of Chemistry Lecture*, " Change of Scale of Chemical Reaction," by Dr. S. J. Green; April 29th, at the United College, St. Andrews, *Centenary Lecture*, " The Story of the *iso*Quinoline Alkaloids," by Dr. R. H. Manske; May 6th, at University College, Dundee, *Lecture*, " The Relation between Theory and Experiment in Physical Chemistry," by Professor E. A. Guggenheim; November 5th, joint meeting with the St. Andrews University Chemical Society, at United College, *Lecture*, " The Physical Chemical Nature of Muscle Elasticity," by Professor A. V. Hill; November 19th, joint meeting with the St. Andrews University Chemical Society, at United College, " Chemicals from Petroleum," by Dr. A. McLean.

Sheffield. At the University, January 29th, joint meeting with the Sheffield University Chemical Society, *Lecture*, " Electron Diffraction in Gases applied to Inorganic Chemistry," by Dr. L. E. Sutton; February 11th, joint meeting with the Sheffield University Chemical Society, *Lecture*, " Modern Fluorine Chemistry," by Dr. R. N. Haszeldine; March 4th, *Official Meeting and Lecture*, " Organic Reactions of Nitrous Acid," by Professor C. K. Ingold; October 21st, joint meeting with the Sheffield University Chemical Society, *Lecture*, " The Polymerisation of Sulphur," by Dr. G. Gee; November 18th, joint meeting with the Sheffield University Chemical Society and the Royal Institute of Chemistry, *Lecture*, " The Regulation of Plant Growth with Chemicals," by Professor R. L. Wain.

Southampton. At the University: February 12th, joint meeting with the University Chemical Society and the Royal Institute of Chemistry, *Lecture*, " Photochemical and Spectroscopic Methods of Studying Fast Reactions," by Professor R. G. W. Norrish. Joint meetings with the University Chemical Society: February 26th, *Lecture*, " The Chemical Nature of Some Metal Alkyls," by Professor G. E. Coates; May 7th, *Lecture*, " The Stereochemistry of *cyclo*Hexane Derivatives," by Professor D. H. R. Barton; October 29th, joint meeting with the University Chemical Society and the Royal Institute of Chemistry, *Lecture*, " Fluorocarbon Chemistry," by Dr. R. N. Haszeldine; November 26th, *Tilden Lecture*, " Molecular Rearrangements," by Professor M. J. S. Dewar.

South Wales. January 15th, joint meeting with the University College of Swansea Chemical Society, at University College, Swansea, *Lecture*, " Some Recent Developments in Theoretical Organic Chemistry," by Professor M. J. S. Dewar; January 25th, at University College, Cardiff, *Lecture*, " Radiation Chemistry," by Professor F. S. Dainton; February

15th, at University College, Cardiff, *Lecture*, " Recent Work on Organic Inclusion Compounds and their Uses," by Professor W. Baker; April 26th, joint meeting with the University College of Swansea Chemical Society and the Royal Institute of Chemistry, at the University College, Swansea, *Lecture*, "Some Reactions of Free Radicals," by Professor W. A. Noyes, jun.; October 18th, at University College, Cardiff, *Lecture*, " Some Applications of Electron Diffraction to Problems in Inorganic Chemistry," by Dr. L. E. Sutton; October 29th, joint meeting with the University College of Swansea Chemical Society, at University College, Swansea, *Lecture*, " Shapes of Molecules," by Dr. J. W. Linnett; November 12th, joint meeting with the University College of Swansea Chemical Society and the Royal Institute of Chemistry, at University College, Swansea, *Lecture*, " Reactions of Some Organic Cations," by Professor H. Burton; November 22nd, at University College, Cardiff, *Lecture*, " The Chemistry of Allenic Systems," by Professor E. R. H. Jones.

APPENDIX B.

ANNUAL REPORT OF THE JOINT LIBRARY COMMITTEE FOR THE YEAR 1954.

In March the Librarian, Mr. A. E. Cummins, was taken seriously ill, and this led to his resignation in September. The vacancy so caused has now been filled by Mr. R. G. Griffin, F.L.A., formerly Librarian of the Brewing Industry Research Foundation.

A report on the Library was prepared by an independent consultant, Mr. W. J. Bishop. As a result of this report, substantial improvements in Library accommodation are at present under way.

Readers have made very great use of the photocopying service during the past twelve months. The number of book pages copied during 1954 was 5673, as against 2639 the previous year. In addition to this, several hundred Infra-red Spectra Sheets were copied, and sections of the staff were also supplied with a great deal of photocopied material. There is some evidence to show that the considerably greater use of the photocopying service is related to the publication of *Current Chemical Papers* and to the fall in the number of readers attending the Library.

Analysis

			Additions.		
	Attendances.	Books borrowed.	Books.	Volumes of periodicals.	Pamphlets.
1954	9,370	7706 (3000 by post)	410	886	69
1953	10,140	8304 (3326 by post)	362	815	143

A number of gifts have been made to the Library during the year, and the Committee tenders its grateful thanks to those Fellows and Publishers who have helped the Library in this way.

THE CHEMICAL SOCIETY

INCOME AND EXPENDITURE ACCOUNTS for the Year ended 31st December, 1954.

GENERAL PURPOSES.

1953 £ s. d.	1953 £ s. d.	*Income.*	1954 £ s. d.	1954 £ s. d.	1954 £ s. d.
20,539 18 0		Separate Subscriptions—			
269 5 5		On account of 1954	21,117 4 2		
		On account of 1953 and previous years	414 4 2		
16,048 17 1		Joint Subscriptions—			
49 16 9		On account of 1954	16,161 16 1		
		On account of 1953 and previous years	113 9 9		
37,507 17 5			37,806 14 2		
1,292 18 0		*Add* Income Tax recovered on Subscriptions under Covenant	1,304 10 4		
	38,800 15 5			39,111 4 6	
	970 12 0	Dividends on Investments		1,192 12 5	
	102 4 9	Donations...		41 9 8	
	420 0 4	Miscellaneous Receipts		756 11 6	
	£40,293 12 4			£41,101 19 1	

1953 £ s. d.	1953 £ s. d.	*Expenditure.*	1954 £ s. d.	1954 £ s. d.
		Administration Expenses :		
5,231 1 7		Salaries, Wages, Superannuation, etc.	5,281 2 4	
617 18 11		House Expenses, etc.	598 10 1	
579 0 6		Office Expenses and Stationery ...	891 2 11	
284 19 9		Postages	272 9 8	
347 18 2		Furniture	405 6 9	
557 12 7		Miscellaneous	539 16 9	
	7,618 12 6			7,788 8 6
	1,329 3 8	Expenses of Conjoint Chemical Office ...		877 14 4
	26 15 0	Subscriptions		46 15 0
	988 3 10	Expenses of Meetings		978 13 10
	526 0 9	Expenses of Local Representatives ...		554 8 4
	518 13 4	Travelling Expenses		448 9 11
18,081 16 2		Transfers to :		
		Publications Account	22,306 15 6	
2,490 0 1		Library Account :		
912 10 10		Capital Expenditure	2,827 9 5	
		Maintenance	1,010 17 8	
3,000 0 0		Special Reserve Fund :		
1,000 0 0		Publications Reserve	— — —	
1,500 0 0		Building and Equipment Reserve...	— — —	
2,000 0 0		Investments Reserve	— — —	
	28,984 7 1	Staff Pensions Fund	800 0 0	
				37,143 2 7
	291 16 2	Balance, being Excess of Income over Expenditure, carried to Balance Sheet		3,262 6 7
	£40,293 12 4			£41,101 19 1

Income and Expenditure Accounts for the Year ended 31st December, 1954.

PUBLICATIONS.

1953 £ s. d.	1953 £ s. d.	*Income.*	1954 £ s. d.	1954 £ s. d.
		Publication Sales (including back numbers):		
23,817 17 5		Journal and Proceedings	24,402 18 9	
2,383 13 5		Annual Reports on Progress of Chemistry	2,528 15 10	
1,919 9 2		Quarterly Reviews	1,978 16 7	
— — —		Current Chemical Papers	1,938 9 4	
2,139 16 5		Authors' Extra Reprints	2,014 3 3	
269 14 6		Other Publications	63 0 1	
	30,230 11 0			32,926 3 10
		Proceeds of Advertisements:		
1,172 10 9		Journal	1,042 12 1	
182 4 5		Annual Reports	194 15 9	
36 12 4		Quarterly Reviews	26 9 6	
— — —		Current Chemical Papers	75 4 9	
	1,391 7 6			1,359 2 1
	367 14 0	Dividends on Investments		367 14 0
		Grants:		
3,800 0 0		Government Publications Grant (through the Royal Society)		— — —
16,600 0 0		The Chemical Council		— — —
	20,100 0 0			
	10 0	Donation		— — —
	18,081 16 2	Transfer from General Purposes Account		22,506 15 6
	£70,171 18 8			£57,159 15 5

1953 £ s. d.	1953 £ s. d.	*Expenditure.*	1954 £ s. d.	1954 £ s. d.
		Expenses on account of Journal:		
5,831 1 2		Salaries, Wages, Superannuation, etc.	6,522 8 11	
22,922 5 5		Printing	24,310 12 6	
7,041 4 1		Paper	6,925 11 8	
3,932 6 6		Banding and Distribution	3,806 5 7	
3,403 7 5		Authors' Reprints	3,675 17 11	
387 4 5		Furniture	21 19 8	
241 6 7		Office Expenses and Stationery ...	393 15 6	
201 15 5		Postages	218 8 2	
162 10 5		Travelling Expenses	220 8 6	
419 7 2		Miscellaneous	439 4 1	
	44,542 8 7			46,534 12 6
	3,763 6 9	Annual Reports on the Progress of Chemistry		3,253 2 3
	3,674 11 10	Quarterly Reviews		3,411 11 6
	391 11 6	Current Chemical Papers		3,880 9 2
		Bureau of Abstracts:		
15,800 0 0		Balance of Grants 1952 and 1953 ...		— — —
2,000 0 0		Provision for Final Liability		— — —
	17,800 0 0			
	£70,171 18 8			£57,159 15 5

INCOME AND EXPENDITURE ACCOUNTS FOR THE YEAR ENDED 31ST DECEMBER, 1954.

LIBRARY.

1953 £ s. d.	1953 £ s. d.	*Income.*	1954 £ s. d.	1954 £ s. d.
	2,490 0 1	Contributions for Books, Periodicals, Binding, Fittings, and Furniture: Transfer from General Purposes Account...		2,827 9 5
		Contributions towards maintenance through the Chemical Council:		
912 10 10		Chemical Society (General Purposes Account)	1,010 17 8	
2,069 5 9		Royal Institute of Chemistry	2,292 5 9	
679 1 1		Society of Chemical Industry	752 4 7	
248 9 9		Faraday Society	275 5 4	
128 10 6		Society for Analytical Chemistry	142 7 6	
246 6 11		Biochemical Society	272 17 11	
711 13 11		Chemical Council (Direct Grant)	821 11 10	
	4,995 18 9			5,567 10 7
		Contributions from other sources:		
100 0 0		Association of British Chemical Manufacturers	100 0 0	
50 0 0		Institute of Brewing	50 0 0	
10 10 0		Society of Dyers and Colourists	10 10 0	
19 15 1		Miscellaneous		
	180 5 1			160 10 0
	£7,666 3 11			£8,555 10 0

1953 £ s. d.	1953 £ s. d.	*Expenditure.*	1954 £ s. d.	1954 £ s. d.
		Capital Expenditure:		
1,213 13 6		Books and Periodicals *	1,743 0 3	
1,199 18 2		Binding...	1,045 9 10	
76 8 5		Furniture	38 19 4	
	2,490 0 1			2,827 9 5
		Maintenance:		
4,551 1 1		Salaries, Wages, Superannuation, etc. ...	4,458 12 6	
— — —		Re-binding	614 7 6	
73 2 7		Postages	76 6 0	
265 15 0		House Expenses, etc.	315 1 8	
164 4 7		Office Expenses and Stationery	168 19 0	
22 0 7		Miscellaneous	94 13 11	
	5,176 3 10			5,728 0 7
	£7,666 3 11			£8,555 10 0

* Other than those received in exchange.

Income and Expenditure Accounts for the Year ended 31st December, 1954.

SPECIAL RESERVE FUND.

1953	*Income.*	1954	1953	*Expenditure.*	1954
£ s. d.		£ s. d.	£ s. d.		£ s. d.
216 3 6	Dividends on Investments	269 8 4		Balance, being Excess of Income over Expenditure, carried to Balance	
201 12 0	Deposit Interest	142 9 8	417 15 6	Sheet	411 18 0
£417 15 6		£411 18 0	£417 15 6		£411 18 0

SPECIAL PUBLICATIONS FUND.

£ s. d.		£ s. d.	£ s. d.		£ s. d.
301 13 0	Sales of Publications and Royalties received	576 14 10	215 13 5	Cost of Publications	332 10 6
69 18 2	Dividends on Investments	77 8 2	17 7 8	Miscellaneous	21 9 5
77 1 7	Deposit Interest	80 14 9		Balance, being Excess of Income over Expenditure, carried to Balance	
			215 11 8	Sheet	380 17 10
£448 12 9		£734 17 9	£448 12 9		£734 17 9

STAFF PENSIONS FUND.

£ s. d.		£ s. d.	£ s. d.		£ s. d.
2,048 8 10	Transfer from General Purposes Account and Refund of Premiums	826 0 9	807 8 4	Pensions	855 13 4
81 17 4	Dividends on Investments	99 8 7	4 14 9	Miscellaneous	3 18 2
12 18 4	Deposit Interest	18 15 0		Balance, being Excess of Income over Expenditure, carried to Balance	
			1,332 1 5	Sheet	82 12 10
£2,144 4 6		£944 4 4	£2,144 4 6		£944 4 4

INCOME AND EXPENDITURE ACCOUNTS FOR THE YEAR ENDED 31ST DECEMBER, 1954.

CENTENARY FUND.

1953	*Income.*	1954	1953	*Expenditure.*	1954
£ s. d.		£ s. d.	£ s. d.		£ s. d.
825 4 7	Dividends on Investments ...	878 11 9	712 15 5	Expenses of Lecturers & Delegates ...	548 15 0
			41 5 2	Miscellaneous ...	43 18 7
			71 6 0	Balance, being Excess of Income over Expenditure, carried to Balance Sheet ...	285 18 2
£825 4 7		£878 11 9	£825 4 7		£878 11 9

CORDAY–MORGAN MEDAL AND PRIZE FUND.

£ s. d.		£ s. d.	£ s. d.		£ s. d.
285 13 2	Dividends on Investments ...	305 13 11	157 10 0	Prize ...	157 10 0
1 18 6	Deposit Interest ...	18 2	7 10 0	Medal ...	6 0 0
			29 6 7	Miscellaneous ...	29 14 7
			91 5 1	Balance, being Excess of Income over Expenditure, carried to Balance Sheet ...	113 7 6
£285 11 8		£306 12 1	£285 11 8		£306 12 1

CORDAY–MORGAN MEMORIAL FUND.

£ s. d.		£ s. d.	£ s. d.		£ s. d.
531 9 1	Dividends on Investments ...	526 6 3	400 0 0	Grant to the Corday–Morgan Memorial Fund Executive ...	400 0 0
			4 10 0	Memorial Expenses (Clause 12 of the Will) ...	6 7 3
			26 2 8	Miscellaneous ...	26 6 4
			100 16 5	Balance, being Excess of Income over Expenditure, carried to Balance Sheet ...	93 12 8
£531 9 1		£526 6 3	£531 9 1		£526 6 3

INCOME AND EXPENDITURE ACCOUNTS FOR THE YEAR ENDED 31ST DECEMBER, 1954.

FARADAY LECTURE FUND.

1953	*Income.*	1954	1953	*Expenditure.*	1954
£ s. d.		£ s. d.	£ s. d.		£ s. d.
15 8 8	Dividend on Investment	15 8 8	26 5 0	Honorarium	— — —
15 14 9	Balance, being Excess of Expenditure over Income, carried to Balance Sheet	— — —	4 3 0	Medal	— — —
			15 5	Miscellaneous	15 5
			— — —	Balance, being Excess of Income over Expenditure, carried to Balance Sheet	14 13 3
£31 3 5		£15 8 8	£31 3 5		£15 8 8

ROBERT JOHN FLINTOFF TRUST.

£ s. d.		£ s. d.	£ s. d.		£ s. d.
34 13 8	Dividends on Investments	34 13 8	— — —	Honorarium	75 0 0
— — —	Balance, being Excess of Expenditure over Income, carried to Balance Sheet	44 16 9	— — —	Medal	2 14 3
			1 14 8	Miscellaneous	1 16 2
			32 19 0	Balance, being Excess of Income over Expenditure, carried to Balance Sheet	— — —
£34 13 8		£79 10 8	£34 13 8		£79 10 8

EDWARD FRANK HARRISON MEMORIAL TRUST.

£ s. d.		£ s. d.	£ s. d.		£ s. d.
46 16 10	Dividends on Investments	46 16 10	— — —	Prize	105 0 0
— — —	Balance, being Excess of Expenditure over Income, carried to Balance Sheet	78 10 0	— — —	Plaque	18 0 0
			24 14 10	Miscellaneous	2 6 10
			22 2 0	Balance, being Excess of Income over Expenditure, carried to Balance Sheet	— — —
£46 16 10		£125 6 10	£46 16 10		£125 6 10

INCOME AND EXPENDITURE ACCOUNTS FOR THE YEAR ENDED 31ST DECEMBER, 1954.

RESEARCH FUND.

1953	*Income.*	1954	1953	*Expenditure.*	1954
£ s. d.		£ s. d.	£ s. d.		£ s. d.
749 16 0	Dividends on Investments	749 16 0	734 14 6	Grants awarded	744 10 0
6 6	Deposit Interest	2 18 10	— — —	Honorarium, Hugo Müller Lecture	21 0 0
63 0 5	Grants repaid or not claimed	63 5 0	52 19 7	Miscellaneous	93 16 8
— — —	Balance, being Excess of Expenditure over Income, carried to Balance Sheet	43 6 10	25 8 10	Balance, being Excess of Income over Expenditure, carried to Balance Sheet	— — —
£813 2 11		£859 6 8	£813 2 11		£859 6 8

SPECIAL LECTURES FUND.

£ s. d.		£ s. d.	£ s. d.		£ s. d.
50 1 10	Dividend on Investment	50 1 10	26 5 0	Honorarium	26 5 0
			2 10 1	Miscellaneous	2 10 1
			21 6 9	Balance, being Excess of Income over Expenditure, carried to Balance Sheet	21 6 9
£50 1 10		£50 1 10	£50 1 10		£50 1 10

TILDEN LECTURE FUND.

£ s. d.		£ s. d.	£ s. d.		£ s. d.
71 5 0	Dividends on Investments	71 5 0	31 10 0	Honorarium	15 15 0
11 6	Deposit Interest	5 9	— — —	Lecture Expenses	20 11 6
			3 11 10	Miscellaneous	3 11 6
			36 14 8	Balance, being Excess of Income over Expenditure, carried to Balance Sheet	31 12 9
£71 16 6		£71 10 9	£71 16 6		£71 10 9

THE CHEMICAL SOCIETY

BALANCE SHEETS, 31st December, 1954.

GENERAL PURPOSES.

1953 £ s. d.	1953 £ s. d.	*Liabilities.*	1954 £ s. d.	1954 £ s. d.
		Sundry Creditors and Credit balances:		
18,790 3 9		Printing and Miscellaneous	15,451 11 9	
12,864 0 10		Fellowship Subscriptions in advance	8,017 14 2	
14,057 11 5		Publications sold in advance	26,031 5 1	
5,500 0 0		Special Reserve Fund...	— — —	
1,200 0 0		Staff Pensions Fund	— — —	
400 0 0		Provision for Special Purposes	400 0 0	
	52,811 16 0			49,900 11 0
		Excess of Assets over Liabilities as per		
27,021 9 3		last Balance Sheet	27,493 5 5	
180 0 0		*Add* Life Composition Fees	501 12 0	
— — —		Perkin Legacy	4,305 19 4	
		Excess of Income over Expenditure for year	3,262 6 7	
291 16 2				
27,493 5 5			35,563 3 4	
		Deduct Net loss on change of Investments	— — —	
764 16 0				
		Add Transfer from Special Reserve Fund	— — —	
764 16 0				
		Net profit on change of Investments	213 6 3	
— — —				
	27,493 5 5			35,776 9 7
	£80,305 1 5			£85,677 0 7

1953 £ s. d.	*Assets.*	1954 £ s. d.
28,391 6 6	Investments as per Schedule (cost or value when acquired)	38,755 3 11
	Sundry Debtors (including payments in advance and postage stamps	
13,295 5 5	in hand)	14,448 12 3
4,253 5 4	Stock of Paper and Wrappers	4,953 12 6
34,365 4 2	Balance at Bank (including Deposit) and Cash in hand	27,519 11 11
£80,305 1 5		£85,677 0 7

BALANCE SHEETS, 31ST DECEMBER, 1954.

PUBLICATIONS FUND.

1953	*Liabilities.*	1954	1953	*Assets.*	1954
£ s. d.		£ s. d.	£ s. d.		£ s. d.
8 2 0	Sundry Creditors	24 6 0	8 2 0	Sundry Debtors	24 6 0
10,978 19 7	Excess of Assets over Liabilities as per last Balance Sheet	10,978 19 7	10,978 19 7	Investments as per Schedule (cost or value when acquired)	10,978 19 7
£10,987 1 7		£11,003 5 7	£10,987 1 7		£11,003 5 7

SPECIAL RESERVE FUND.

£ s. d.	£ s. d.		£ s. d.	£ s. d.		£ s. d.
	764 16 0	Sundry Creditors		5 14 8	Sundry Debtors	48 8 4
		Publications Reserve:			Investments as per Schedule (cost or value when acquired)	17,821 12 11
9,585 0 7		As per last Balance Sheet	12,585 0 7		Balances at Bank (including Deposit) and on Deposit in London Trustee Savings Bank	6,474 10 9
3,000 0 0		*Add* Transfer from General Purposes Account	— — —			
	12,585 0 7		12,585 0 7			
	1,309 17 8	Library Reserve: As per last Balance Sheet	1,309 17 8			
		Building and Equipment Reserve:				
3,025 0 0		As per last Balance Sheet	4,025 0 0			
1,000 0 0		*Add* Transfer from General Purposes Account	— — —			
	4,025 0 0		4,025 0 0			
		Investments Reserve:				
2,100 0 0		As per last Balance Sheet	2,835 4 0			
		Deduct Transfer to General Purposes Account—net loss on Change of				
764 16 0		Investments	— — —			
1,335 4 0						
1,500 0 0		*Add* Transfer from General Purposes Account	— — —			
	2,835 4 0		2,835 4 0			
		General Purposes Reserve:				
2,714 5 11		Amount brought forward	3,133 1 5			
1 0 0		*Add* Profit on Change of Investments	38 15 8			
417 15 6		Excess of Income over Expenditure for year	411 18 0			
	3,133 1 5		3,583 15 1			
	£24,652 19 8		£24,344 12 0	£24,652 19 8		£24,344 12 0

BALANCE SHEETS, 31ST DECEMBER, 1954.

SPECIAL PUBLICATIONS FUND.

1953 £ s. d.	1953 £ s. d.	*Liabilities.*	1954 £ s. d.	1954 £ s. d.	1953 £ s. d.	1953 £ s. d.	*Assets.*	1954 £ s. d.	1954 £ s. d.
	62 4 5	Sundry Creditors		306 4 7	105 11 9		Sundry Debtors		130 9 9
5,973 7 10		Excess of Assets over Liabilities as per last Balance Sheet	6,188 19 6		2,011 19 10		Investments as per Schedule (cost or value when acquired)		4,010 14 11
215 11 8		*Add* Excess of Income over Expenditure for year	380 17 10		4,133 12 4		Balances at Bank and on deposit in the Post Office Savings Bank and London Trustee Savings Bank		2,734 17 3
	6,188 19 6			6,569 17 4					
	£6,251 3 11			£6,876 1 11	£6,251 3 11				£6,876 1 11

STAFF PENSIONS FUND.

£ s. d.	£ s. d.		£ s. d.	£ s. d.	£ s. d.	£ s. d.		£ s. d.	£ s. d.
	41 14 9	Sundry Creditors		3 18 2	1,200 0 0		Sundry Debtors		26 0 9
3,981 11 5		Excess of Assets over Liabilities as per last Balance Sheet	5,313 12 10		3,572 3 10		Investments as per Schedule (cost or value when acquired)		5,176 0 2
		Add Profit on Change of Investments	11 6 4		583 3 9		Balance on deposit in the Post Office Savings Bank		219 1 8
1,332 1 5		Excess of Income over Expenditure for year	82 12 10						
	5,313 12 10			5,407 12 0					
		Bank Overdraft		7 12 5					
	£5,355 7 7			£5,421 2 7	£5,355 7 7				£5,421 2 7

CENTENARY FUND.

£ s. d.	£ s. d.		£ s. d.	£ s. d.	£ s. d.	£ s. d.		£ s. d.	£ s. d.
	61 19 11	Sundry Creditors		43 18 7	412 3 4		Sundry Debtors		1,041 2 1
		Capital Account:			27,698 3 4		Investments as per Schedule (cost or value when acquired)		27,698 3 4
25,531 1 0		As per last Balance Sheet	28,076 1 11		145 1 9		Balance at Bank		813 9 6
2,545 0 11		*Add* Contributions under Deeds and Donations for year	1,029 9 8						
	28,076 1 11			29,105 11 7					
		Income Account:							
46 0 7		Amount brought forward	117 6 7						
71 6 0		*Add* Excess of Income over Expenditure for year	285 18 2						
	117 6 7			403 4 9					
	£28,255 8 5			£29,552 14 11	£28,255 8 5				£29,552 14 11

BALANCE SHEETS, 31ST DECEMBER, 1954.

CORDAY-MORGAN MEDAL AND PRIZE FUND.

1953			*Liabilities.*	1954			1953			*Assets.*	1954		
£	s.	d.		£	s.	d.	£	s.	d.		£	s.	d.
			Sundry Creditors		15	6				Sundry Debtors	161	18	0
	80	19	2				6,858	3	2	Investments as per Schedule (cost or value when acquired)...	7,370	19	7
			Capital Account :				642	1	11	Balance at Bank	93	1	6
5,885	9	8	As per last Balance Sheet	5,885	9	8							
—	—	—	*Add* Net Profit on change of Investments...	12	16	5							
	5,885	9	8		5,898	6	1						
			Income Account :										
1,507	13	10	As per last Balance Sheet	1,598	18	11							
91	5	1	*Add* Excess of Income over Expenditure for year	113	7	6							
	1,598	18	11		1,712	6	5						
	£7,565	7	9		£7,625	19	1	£7,565	7	9	£7,625	19	1

CORDAY-MORGAN MEMORIAL FUND.

£	s.	d.	£	s.	d.		£	s.	d.	£	s.	d.		£	s.	d.
			31	1	5	Sundry Creditors				432	13	7	Sundry Debtors	235	5	7
						Capital Account :							Investments as per Schedule (cost or value when acquired)	12,239	5	10
10,090	2	8				As per last Balance Sheet	10,091	19	1				Balance at Bank	933	19	9
—	—	—				*Add* Profit on change of Investments	11	14	5							
						Balance on Bonus Issue of Barclays Bank Ltd., " B " Ordinary Stock	—	—	—							
1	16	5														
			10,091	19	1					10,103	13	6				
						Income Account:										
2,677	15	0				As per last Balance Sheet	2,778	11	5							
100	16	5				*Add* Excess of Income over Expenditure for year	93	12	8							
			2,778	11	5					2,872	4	1				
	£12,901	11	11					£13,408	11	2	£12,901	11	11	£13,408	11	2

BALANCE SHEETS, 31ST DECEMBER, 1954.

FARADAY LECTURE FUND.

1953 £ s. d.		1953 £ s. d.	
	Liabilities.		*Assets.*
	Sundry Creditors	15 5	Investments as per Schedule (cost or value when acquired)
502 3 4	Excess of Assets over Liabilities as per last Balance Sheet	486 8 7	
— — —	*Add* Excess of Income over Expenditure for year	14 13 3	
15 14 9	*Deduct* Excess of Expenditure over Income for year	— — —	
		501 1 10	
		£501 17 3	

1953 £ s. d.		1954 £ s. d.
	Assets.	
439 4 0	Investments as per Schedule (cost or value when acquired)	469 4 0
48 0 0	Balance at Bank	32 13 3
£487 4 0		£501 17 3

ROBERT JOHN FLINTOFF TRUST.

1953 £ s. d.		1954 £ s. d.	
	Liabilities.		*Assets.*
	Sundry Creditors	1 14 8	Sundry Debtors
1,078 0 6	Excess of Assets over Liabilities as per last Balance Sheet	1,110 19 6	
32 19 0	*Add* Excess of Income over Expenditure for year	— — —	
— — —	*Deduct* Excess of Expenditure over Income for year	44 16 9	
1,110 19 6		1,066 2 9	
£1,112 14 2		£1,067 17 5	

1953 £ s. d.		1954 £ s. d.
	Assets.	
5 2 0	Sundry Debtors	3 8 0
1,000 0 0	Investments as per Schedule (cost or value when acquired)	1,000 0 0
107 12 2	Balance at Bank	64 9 5
£1,112 14 2		£1,067 17 5

EDWARD FRANK HARRISON MEMORIAL TRUST.

1953 £ s. d.		1954 £ s. d.	
	Liabilities.		*Assets.*
	Sundry Creditors	12 0 5	Investments as per Schedule (cost or value when acquired)
1,182 5 5	Excess of Assets over Liabilities as per last Balance Sheet	1,204 7 8	
22 2 0	*Add* Excess of Income over Expenditure for year	— — —	
— — —	*Deduct* Excess of Expenditure over Income for year	78 10 0	
1,204 7 8		1,125 17 8	
£1,206 14 6		£1,137 18 1	

1953 £ s. d.		1954 £ s. d.
	Assets.	
1,101 7 11	Investments as per Schedule (cost or value when acquired)	1,101 7 11
105 6 7	Balance at Bank	36 10 2
£1,206 14 6		£1,137 18 1

Balance Sheets, 31st December, 1954.

RESEARCH FUND.

1953 £ s. d.	1953 £ s. d.	*Liabilities.*	1954 £ s. d.	1954 £ s. d.	1953 £ s. d.	*Assets.*	1954 £ s. d.
	824 18 7	Sundry Creditors		869 14 10	27 0 0	Sundry Debtors	81 0 0
23,986 18 4		Excess of Assets over Liabilities as per last Balance Sheet	22,982 7 2		23,923 4 7	Investments as per Schedule (cost or value when acquired)	23,923 4 7
25 8 10		*Add* Excess of Income over Expenditure for year	— — —		857 1 2	Balance at Bank (including Deposit) and on deposit in Post Office Savings Bank	804 10 7
— — —		*Deduct* Excess of Expenditure over Income for year	43 6 10				
	23,982 7 2			22,939 0 4			
	£24,807 5 9			£24,808 15 2	£24,807 5 9		£24,808 15 2

SPECIAL LECTURES FUND.

£ s. d.	£ s. d.		£ s. d.	£ s. d.	£ s. d.		£ s. d.
	2 10 1	Sundry Creditors		2 10 1	1,615 5 0	Investment as per Schedule (cost or value when acquired)	1,615 5 0
1,702 8 7		Excess of Assets over Liabilities as per last Balance Sheet	1,723 15 4		111 0 5	Balance at Bank	132 7 2
21 0 9		*Add* Excess of Income over Expenditure for year	21 0 9				
	1,723 15 4			1,745 2 1			
	£1,726 5 5			£1,747 12 2	£1,726 5 5		£1,747 12 2

TILDEN LECTURE FUND.

£ s. d.	£ s. d.		£ s. d.	£ s. d.	£ s. d.		£ s. d.
	3 11 10	Sundry Creditors		3 11 6	10 1 7	Sundry Debtors	27 5 5
2,023 18 3		Excess of Assets over Liabilities as per last Balance Sheet	2,060 12 11		1,878 14 10	Investments as per Schedule (cost or value when acquired)	1,978 14 10
36 14 8		*Add* Excess of Income over Expenditure for year	31 12 9		175 8 4	Balance at Bank	89 16 11
	2,060 12 11			2,092 5 8			
	£2,064 4 9			£2,095 17 2	£2,064 4 9		£2,095 17 2

MICHAEL W. PERRIN, *Honorary Treasurer.*

We have examined the above Balance Sheets and accompanying Income and Expenditure Accounts with the Books and Vouchers of the Society, and certify them to be in accordance therewith and, in our opinion, correct. We have also verified the Balances at the Bankers and Investments.

FINSBURY CIRCUS HOUSE,
BLOMFIELD STREET, E.C.2
17th MARCH, 1955.

W. B. KEEN & CO.
Chartered Accountants.

SCHEDULE OF INVESTMENTS.

GENERAL PURPOSES.

Nominal Details.	*Cost or Value when Acquired.*	*Market Value 31st December, 1954.*
	£ s. d.	£
£2,609 14s. 4d. 3½% Conversion Loan, 1961, or after	2,044 16 0	2,310
£2,000 3% Savings Bonds, 1965/75	2,006 4 5	1,880
£1,000 3% Funding Loan, 1959/69	973 6 6	970
£5 5½% Defence Bonds (Conversion Issue)	5 0 0	5
£1,000 3½% Defence Bonds	1,000 0 0	1,000
£195 3% Defence Bonds, 3rd Issue	194 7 0	195
£4,747 4s. 6d. 3% British Transport Guaranteed Stock, 1978/88 ...	5,704 9 8	4,154
£2,546 1s. 4d. 3% British Electricity Guaranteed Stock, 1968/73 ...	2,549 4 5	2,419
£2,425 8s. 9d. 3% Commonwealth of Australia Registered Stock, 1964/66	2,434 10 8	2,316
£A3,000 3½% Commonwealth of Australia Treasury Bonds, 1961/64	2,552 16 7	2,145
£1,000 4% Canadian Pacific Railway Perp. Deb. Stock	838 8 9	880
£766 3½% London Trust Co., Ltd., Red. Deb. Stock	576 2 9	601
£1,000 4% Rolls-Royce, Ltd., Red. Deb. Stock, 1974/84	1,007 1 9	1,015
£925 4% Olympia, Ltd., 1st Mort. Red. Deb. Stock	853 9 3	819
£1,000 5½% Wankie Colliery Co., Ltd., Mort. Deb. Stock	1,149 3 9	1,160
800 Rotary Hoes, Ltd., 6% Red. Cum. Pref. £1 Shares	839 16 0	800
780 Scottish and Mercantile Investment Co., Ltd., 7½% Cum. Pref. £1 Shares	940 8 5	938
£800 8% British Petroleum Co., Ltd., Cum. First Pref. Stock	778 16 6	844
1,000 5% Bell London & Provincial Props. Ltd., Cum. Pref. £1 Shares	884 1 6	900
900 6½% J. & N. Phillips & Co., Ltd., Cum. Pref. £1 Shares	929 14 0	968
1,000 5% Geo. Sandeman & Sons, Ltd., Cum. Pref. £1 Shares	938 1 6	1,038
160 Allen & Hanburys, Ltd., Ord. £1 Shares	521 6 6	455
£440 Cable & Wireless (Holding), Ltd., Ord. Stock	549 6 6	908
£50 Commercial Union Assurance Co., Ltd., Stock	580 13 6	838
£300 Goodlass Wall & Lead Industries, Ltd., Ord. Stock	496 9 6	878
£145 Leyland Motors, Ltd., Ord. Stock...	702 9 2	739
£180 Shell Transport and Trading Co., Ltd., Ord. Stock	665 12 6	1,074
£320 Peninsular and Oriental Steam Navigation Co., Ltd., Def. Stock	504 4 6	976
£200 Tube Investment Trust, Ltd., Ord. Stock	700 11 6	813
1,500 Home and Colonial Stores, Ltd., Ord. 6s. 8d. Shares	794 9 0	938
£330 British Insulated Callender's Cables, Ltd., Ord. Stock	783 11 6	800
500 Trust Houses, Ltd., Ord. £1 Shares	700 5 3	713
£400 Charterhouse Investment Trust, Ltd., Ord. Stock	727 16 6	730
600 Consolidated Zinc Corporation, Ltd., Ord. £1 Shares	939 15 3	1,313
£300 Smiths Stamping Works (Coventry), Ltd., Ord. Stock	888 13 10	750
	£38,755 3 11	£39,282

PUBLICATIONS FUND.

£2,260 19s. 9d. 3½% Conversion Loan, 1961, or after	1,566 16 4	2,001
£1,000 3% Savings Bonds, 1955/65	1,000 0 0	1,000
£2,261 1s. 11d. 3% Savings Bonds, 1960/70...	2,276 1 11	2,171
£2175 13s. 4d. 3% British Transport Guaranteed Stock, 1978/88 ...	1,929 1 4	1,904
£2,000 3% British Electricity Guaranteed Stock, 1968/73	2,002 10 0	1,900
£1,200 3% Commonwealth of Australia Registered Stock, 1964/66 ...	1,204 10 0	1,146
£982 12s. 0d. 3% Southern Rhodesia Stock, 1971/73	1,000 0 0	899
	£10,978 19 7	£11,021

SPECIAL RESERVE FUND.

Nominal Details.	*Cost or Value when Acquired*	*Market Value 31st December, 1954.*
	£ s. d.	£
£1,500 3% Savings Bonds, 1955/65	1,489 1 0	1,500
£1,250 3% Funding Loan, 1959/69	1,217 9 9	1,213
£1,165 2½% Funding Loan, 1956/61	1,169 7 5	1,165
£500 3% Defence Bonds, 3rd Issue	496 19 9	500
£1,300 3½% Defence Bonds (Conversion Issue)	1,292 3 3	1,300
£1,000 3% Sheffield Corporation Stock, 1967/69	962 8 6	960
£2,582 10s. 9d. 3% Liverpool Corporation Stock, 1955/58	2,647 2 0	2,583
£1,500 3% Ceylon Stock, 1959/64	1,428 8 6	1,403
£1,000 2½% Agricultural Mortgage Corporation, Ltd., Deb. Stock, 1961/63	1,020 3 0	985
£1,000 3½% Covent Garden Properties, Ltd., Red. Deb. Stock, 1968...	951 5 3	915
£1,000 4% Cable and Wireless (Holding), Ltd., 10 year Red. Unsec. Stock, 1960	1,015 4 9	985
£1,100 4½% Nelson Financial Trust, Ltd., Deb. Stock, 1970	981 14 9	1,007
£1,000 4% Dominion and General Trust, Ltd., Red. Deb. Stock, 1959/64	987 1 6	955
£1,000 4½% Rugby Portland Cement Co., Ltd., Unsec. Stock, 1957/62	1,040 2 6	995
£1,000 5½% Clan Line Steamers, Ltd., Cum. Red. 1st " B " Pref. Stock	1,113 1 0	1,125
	£17,891 13 11	£17,591

SPECIAL PUBLICATIONS FUND.

£745 9s. 2d. 3½% Conversion Loan, 1961, or after	569 0 10	660
£746 1s. 0d. 3% British Transport Guaranteed Stock, 1978/88 ...	719 18 9	653
£750 3% British Electricity Guaranteed Stock, 1968/73	750 18 9	713
£1,000 3½% London County Consolidated Stock, 1968/73...	997 1 6	990
£1,000 4% Government of the Fed. of Rhodesia and Nyasaland Stock, 1972/74	973 15 1	1,015
	£4,010 14 11	£4,031

STAFF PENSIONS FUND.

£119 0s. 1d. 3½% Conversion Loan, 1961, or after	92 14 10	105
£170 3% Savings Bonds, 1955/65	170 0 0	170
£755 3% Defence Bonds, 3rd Issue	750 8 7	755
£1,000 3½% Defence Bonds	1,000 0 0	1,000
£750 3½% Defence Bonds (Conversion Issue)	745 9 3	750
£1,500 3% Sheffield Corporation, Red. Deb. Stock, 1967/69	1,442 3 6	1,440
£1,000 3½% Southern Rhodesia Stock, 1955/65	975 4 0	975
	£5,176 0 2	£5,195

TILDEN LECTURE FUND.

	£ s. d.	£
£419 4s. 10d. 3% Funding Loan, 1959/69	386 12 10	407
£792 10s. 8d. 3% British Transport Guaranteed Stock, 1978/88 ...	725 2 0	693
186 National Provincial Bank Ltd. " B " Shares £5 each, £1 paid ...	678 18 0	763
£220 3% Metropolitan Water Board (Kent Water Works) Deb. Stock	188 2 0	174
	£1,978 14 10	£2,037

SCHEDULE OF INVESTMENTS.

CENTENARY FUND.

Nominal Details.	*Cost or Value when Acquired.*	*Market Value 31st December, 1954.*
	£ s. d.	£
£2,637 10s. 6d. 3½% Conversion Loan, 1961, or after	2,500 0 0	2,331
£2,477 12s. 11d. 3% Savings Bonds, 1955/65	2,491 11 10	2,478
£2,500 3% Savings Bonds, 1960/70	2,534 7 6	2,400
£2,705 16s. 7d. 2½% Savings Bonds, 1964/67	2,500 0 0	2,571
£2,279 13s. 0d. 3% British Transport Guaranteed Stock, 1978/88 ...	2,237 7 9	1,995
£2,500 3% British Electricity Guaranteed Stock, 1968/73	2,498 8 9	2,375
£4,933 15s. 11d. 4% Consolidated Stock, 1957, or after	4,500 0 0	4,761
£2,302 19s. 6d. 3½% Agricultural Mortgage Corporation Ltd. Deb. Stock, 1975/78	2,000 0 0	2,199
£1,970 1s. 0d. 3% New Zealand Stock, 1973/77	2,000 0 0	1,842
£1,716 15s. 2d. 3½% Northern Ireland Stock, 1969/71	1,700 0 0	1,651
£A3,500 3½% Commonwealth of Australia Treasury Bonds, 1961/64	2,936 7 6	2,503
	£27,698 3 4	£27,089

CORDAY-MORGAN MEDAL AND PRIZE FUND.

£1,951 8s. 2d. 3½% War Loan, 1952, or after	1,825 14 0	1,703
£635 3s. 10d. 3% British Transport Guaranteed Stock, 1978/88 ...	574 17 0	558
£640 15s. 5d. 4% Consolidated Stock, 1957, or after	647 11 1	618
£774 6s. 3d. 3% British Guiana Government Stock, 1975/80	690 5 4	662
£137 10s. 0d. 3% Federated Malay States Government Stock, 1960/70	120 6 3	121
£137 10s. 0d. 3½% Bournemouth Corporation Stock Red., 1958/62...	133 14 5	138
£300 3½% Hertfordshire County Red. Stock, 1954/59	297 15 0	305
£112 Barclays Bank (D. C. & O.), "A" Ord. Stock	201 7 6	246
£172 Mitchells & Butlers, Ltd., Ord. Stock	713 16 0	559
£206 Watney Combe Reid & Co., Ltd., Def. Ord. Stock	597 8 0	805
£83 Imperial Tobacco Co. (G.B. & I.) Ltd., Ord. Stock	263 5 0	245
£240 Cardinal Investment Trust, Ltd., Def. Stock	291 0 0	587
£104 Commercial Union Assurance Co., Ltd., Stock	1,014 0 0	1,742
	£7,370 19 7	£8,287

ROBERT JOHN FLINTOFF TRUST.

£523 2s. 2d. 3½% Conversion Loan, 1961, or after	500 0 0	463
£345 19s. 4d. 3% British Transport Guaranteed Stock, 1978/88 ...	500 0 0	478
	£1,000 0 0	£941

EDWARD FRANK HARRISON MEMORIAL TRUST.

£61 15s. 8d. 3½% Conversion Loan, 1961, or after	50 1 5	55
£1,489 10s. 6d. 3% British Transport Guaranteed Stock, 1978/88 ...	1,051 6 6	1,303
	£1,101 7 11	£1,358

CORDAY-MORGAN MEMORIAL FUND.

Nominal Details.	*Cost or Value when Acquired.*	*Market Value 31st December, 1954.*
	£ s. d.	£
£1,530 2s. 8d. 3½% Conversion Loan, 1961, or after	1,426 4 2	1,334
£1,973 16s. 11d. 3½% War Stock, 1952, or after	1,880 1 10	1,722
£477 1s. 10d. 3% British Electricity Guaranteed Stock, 1968/73 ...	430 17 0	453
£1,062 10s. 11d. 3% British Gas Guaranteed Stock, 1990/95	594 5 7	930
£413 13s. 7d. 4% Consolidated Stock, 1957	412 10 0	399
£217 12s. 6d. 3% London County Consolidated Stock, 1962/67 ...	208 7 6	211
£1,035 0s. 7d. 3% Redemption Stock, 1986/96	928 18 10	900
£137 10s. 0d. 4½% Kenya Government Stock, 1961/71	148 16 11	140
£300 3% New Zealand Government Stock, 1952/53	298 10 0	300
£1,000 4% South Staffordshire Waterworks Red. Pref. Stock, 1971	1,046 10 6	955
£300 3½% Hull Corporation Red. Stock, 1973/78	303 15 0	303
£108 Barclays Bank, Ltd., "B" Ord. Stock	237 3 0	267
£309 Benskins Watford Brewery, Ltd., Ord. Stock	684 19 0	898
£206 H. & G. Simmonds, Ltd., Ord. Stock	824 0 0	592
£160 Imperial Tobacco Co. (G.B. & I.) Ltd., Ord. Stock	506 5 0	472
£108 Thomas Tilling, Ltd., Ord. Stock	107 6 6	205
£340 Alliance Trust, Ltd., 4½% Deb. Stock, 1956	344 5 0	352
£69 London & Lancashire Insurance Co., Ltd., Ord. Stock	448 10 0	621
68 Phœnix Assurance Co., Ltd., Ord. £1 Shares	1,088 0 0	1,598
	£12,239 5 10	£12,632

RESEARCH FUND.

£4,177 16s. 1d. 3½% Conversion Loan, 1961, or after	3,625 16 8	3,697
£500 3% Defence Bonds, 4th issue	500 0 0	500
£1,835 2½% Funding Loan, 1956/61	1,835 0 0	1,835
£1,500 3% Savings Bonds, 1955/65	1,515 0 0	1,500
£4,000 3% Savings Bonds, 1960/70	4,060 0 0	3,840
£3,755 2s. 1d. 3% British Transport Guaranteed Stock, 1978/88 ...	3,567 19 5	3,288
£3,719 8s. 2d. 3% British Electricity Guaranteed Stock, 1968/73 ...	3,734 1 2	3,533
£4,000 3% Commonwealth of Australia Registered Stock, 1964/66...	4,015 0 0	3,820
£1,116 7s. 0d. 3% New Zealand Stock, 1973/77	1,080 7 4	1,044
	£23,923 4 7	£23,055

SPECIAL LECTURES FUND.

£1,669 17s. 3d. 3% British Transport Guaranteed Stock, 1978/88 ...	£1,615 5 0	£1,461

FARADAY LECTURE FUND.

£473 8s. 9d. 3½% Conversion Loan, 1961, or after	£469 4 0	£419

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